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BONE MARROW INFUSION AND ITS COMPLICATIONS

J. J. QUILLIGAN Jr., M.D.
ANN ARBOR, MICH.
AND
HENRY TURKEL, M.D.
DETROIT

WITHIN the past few years considerable emphasis has been placed on the bone marrow as a route for parenteral administration of fluids. In this report a method for using the marrow cavity to infuse fluids is described. Some refinements in technic as well as a partial analysis of the ill effects of the method are included. Also, the case of 1 infant, in whom complicating osteomyelitis developed, is presented.

HISTORY

In 1922 Drinker [1] and Doan [2] independently demonstrated by perfusion experiments the adequacy of the bone marrow for infusion of fluids. In 1934 Josefson [3] reported on the use of liver preparations injected into the bone marrow and advised giving fluids by this route. In 1937 Benda and his associates [4] described the use of the bone marrow cavity in guinea pigs and human beings as a route for injection of drugs, bacteria, air emboli and radiopaque substances into the general circulation. Using colloidal thorium dioxide, they demonstrated the

From the Department of Pediatrics and Communicable Diseases, University of Michigan School of Medicine.

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2. Doan, C. A.: The Circulation of the Bone Marrow, Contrib. Embryol. **14**:27, 1922.

3. Josefson, A.: A New Method of Treatment: Intraossal Injections, Acta med. Scandinav. **81**:550, 1934.

4. Benda, R.: Reseignements fournsi par les injections intramédullaires de sang humaine chez le cobaye, Sang **11**:659, 1937. Benda, R.; Debray, C., and Bourrée, J.: Injection du système veineux du cobaye par voie médullaire osseuse: Resultats qu'il est possible d'en attendre, Bull. et mém. Soc. méd. d. hôp. de Paris **53**:662 (May 14) 1937. Benda, R.; Orinstein, E., and Depitre: Injections intra-médullaires osseuses de substances opaques chez l'homme, Sang **14**:172, 1940.

almost immediate appearance of this material in the venous circulation and lungs. In 1940 Henning,[5] injected concentrated blood and bone marrow in the treatment of granulocytopenia. He also demonstrated that radiopaque material when injected into the sternum could be detected in the mammary veins immediately after injection, and he advocated and used this method in peripheral circulatory collapse in human beings. He reported the successful infusion of dextrose, strophanthin, neoarsphenamine and blood through the sternum and also advised this route for transfusions given to battle casualties.

It remained for Tocantins[6] and his associate to reemphasize the existence of an intimate relationship between the bone marrow and the peripheral circulation. Macht,[7] and later others, injected a variety of substances into the tibia, femur and humerus of animals and human

5. Henning, N.: Die intrasternale Injektion als Ersatz für die intravenöse Injektion, Med. Klin. **36**:724 (June) 1940; Die intrasternale Injektion als Ersatz für die intravenöse Injektion, Klin. Wchnschr. **19**:671 (June 29) 1940; Die intrasternale Injektion und Transfusion als Ersatz für die intravenösen Methoden, Deutsche med. Wchnschr. **66**:737 (July 5) 1940; Ueber die intrasternale bzw. intraossale Injektion und Infusion, ibid. **69**:720 (Oct. 15) 1943; abstracted, J. A. M. A. **128**:240 (May 19) 1945.

6. (*a*) Tocantins, L. M.: Rapid Absorption of Substances Injected into the Bone Marrow, Proc. Soc. Exper. Biol. & Med. **45**:292 (Oct.) 1940. (*b*) Tocantins, L. M., and O'Neill, J. F.: Infusion of Blood and Other Fluids into the Circulation Via the Bone Marrow, ibid. **45**:782 (Dec.) 1940. (*c*) Tocantins, L. M.; O'Neill, J. F., and Price, A. H.: Infusions of Blood and Other Fluids Via the Bone Marrow in Traumatic Shock and Other Forms of Peripheral Circulatory Failure, Ann. Surg. **114**:1085 (Dec.) 1941. (*d*) Tocantins, L. M., and O'Neill, J. F.: Infusions of Blood and Other Fluids into the General Circulation Via the Bone Marrow, Surg., Gynec. & Obst. **73**:281 (Sept.) 1941. (*e*) Tocantins, L. M.; O'Neill, J. F., and Jones, H. W.: Infusions of Blood and Other Fluids Via the Bone Marrow-Applications in Pediatrics, J. A. M. A. **117**:1229 (Oct. 11) 1941. (*f*) Jones, H. W.; Tocantins, L. M.; Erf, L. A., and Munro, F. L.: 4x Concentrated Blood Plasma Intrasternally in the Treatment of Shock, Tr. A. Am. Physicians **57**:88, 1942. (*g*) Price, A. H., and Tocantins, L. M.: Light, Compact Unit for Intravenous or Intraosseous Injection of Plasma in Emergencies, Ann. Surg. **117**:152 (Jan.) 1943. (*h*) Tocantins, L. M.: The Administration of Drugs, Blood and Other Fluids Via the Bone Marrow: Practical Aspect, Philadelphia Med. **36-39**:1144 (May 15) 1943. (*i*) Jones, H. W.; Munro, F. L.; Erf, L. A., and Tocantins, L. M.: A Discussion of the Use of Blood and Plasma Transfusion, Delaware State M. J. **14**:137 (June) 1942. (*j*) O'Neill, J. F.; Tocantins, L. M., and Price, A. H.: Further Experiences with the Technique of Administering Blood and Other Fluids Via the Bone Marrow, North Carolina M. J. **3**:495 (Sept.) 1942. (*k*) Tocantins, L. M.; Price, A. H., and O'Neill, J. F.: Infusions Via the Bone Marrow in Children, Pennsylvania M. J. **46**:1267 (Sept.) 1943. (*l*) O'Neill, J. F.; Bauer, D. de F., and Tocantins, L. M.: Osteoclysis for Parenteral Therapy, McGill M. J. **12**:141 (April) 1943.

7. (*a*) Macht, D. I.: Studies on Intraosseous Injections of Epinephrine, Am. J. Physiol. **38**:269 (Jan.) 1943; Experimental Administration of Drugs Through

beings and found that the effects produced were the same as those of injections by the intravenous route. Meyer and Perlmutter [8] observed that the absorption rate of blood injected into the marrow cavity was equal to the absorption rate of blood given intravenously.

The obvious clinical applications of this method were pointed out by many groups of investigators,[9] and some of the reports dealt primarily

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the Bone Marrow, M. Leaves **5**:171, 1943; Experimental Administration of Drugs Through the Marrow, Tr. Am. Therap. Soc. **42**:64, 1942. (*b*) Wile, U., and Schamberg, I. L.: Pulmonary Fat in Embolism Following Infusions Via the Bone Marrow, J. Invest. Dermat. **5**:173 (Aug.) 1942.

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9. (*a*) Benda, R.; Orinstein, E., and Depitre: La methode des injections intramédullaires de substances opaques appliqués a l'étude du sternum, Bull. et mém. Soc. méd. d. hôp. de Paris **56**:117 (May 9) 1940. (*b*) Papper, E. M., and Rovenstine, E. A.: Utility of Marrow Cavity of Sternum for Parenteral Fluid Therapy, War Med. **2**:277 (March) 1942. (*c*) Papper, E. M.: Bone Marrow Route for Injecting Fluids and Drugs into the General Circulation, Anesthesiology **3**:307 (May) 1942. (*d*) Faxon, N. W., and Churchill, E. D.: Cocoanut Grove Disaster in Boston, J. A. M. A. **120**:1385 (Dec. 26) 1942. (*e*) Soutter, L.: Symposium on the Management of the Cocoanut Grove Burns at the Massachusetts General Hospital: A Note on the Blood Bank, Ann. Surg. **117**:928 (June) 1943. (*f*) Ellison, J. B.: Bone Marrow Transfusion, Correspondence, Brit. M. J. **1**:266 (Feb. 19) 1944. (*g*) Morgan, H. V.; Christie, R. V., and Roxburgh, I. A.: Experiences in the Systemic Administration of Penicillin, ibid. **1**:515 (April 15) 1944. (*h*) Behr, G.: Bone Marrow Infusions, ibid. **1**:305 (Feb. 26) 1944. (*i*) Bailey, H.: Bone Marrow as a Site for the Reception of Infusions, Transfusion and Anaesthetic Agents, ibid. **1**:181 (Feb. 5) 1944. (*j*) Ficarra, B. J.: The Evolution of Blood Transfusion, Ann. M. Hist. **43**:302 (July) 1942. (*k*) Jones, R. M.: A New Needle for the Treatment of Shock by Sternal Infusion, Surg., Gynec. & Obst. **76**:587 (May) 1943. (*l*) Turkel, H., and Bethell, F. H.: A New and Simple Instrument for Administration of Fluids Through Bone Marrow, War Med. **5**:222 (April) 1944; (*m*) Biopsy of Bone Marrow Performed by a New and Simple Instrument, J. Lab. & Clin. Med. **28**:1246 (July) 1943. (*n*) Doud, E. A., and Tysell, J. E.: Massive Intramedullary Infusions, J. A. M. A. **120**:1212 (Dec. 12) 1942. (*o*) Shock: Its Nature and Therapy, U. S. Nav. M. Bull. **41**:93 (Jan.) 1943. (*p*) Harkins, H. J.: Treatment of Shock from War Wounds, Illinois M. J. **83**:325 (May) 1943. (*q*) Peet, M. M., and Campbell, K. N.: Massive Chylothorax Following Splanchnicectomy: Treatment with Intravenous and Intrasternal Transfusions of Chyle, Univ. Hosp. Bull., Ann Arbor **9**:2 (Jan.) 1943. (*r*) Lundy, J. S.; Adams, R. C., and Seldon, T. H.: Plasma and Blood in Treatment of Shock from Burns, S. Clin. North America **24**:798 (Aug.) 1944. (*s*) The Treatment of "Wound Shock," Medical Research Council War Memorandum no. 1, ed. 2, London, His Majesty's Stationery Office, 1944, p. 30. (*t*) Churchill, E. D.: Theater Experience in Wounds of the Abdomen: Modern Surgery in Combat Area with Evacuation Based on the Surgical Urgency of the Wounds, M. Bull. North African Theat. Op. (no. 3) **1**:2 (March) 1944. (*u*) Levenson, S. M.; Davison, C. S.; Lund, C. C., and Taylor, F. H. L.: The Nutrition of Patients with Thermal Burns,

(Footnote continued on next page)

with its use for infants and children.[10] Arbeiter and Greengard[10a] have used the intraosseous method for 43 infants with success and Meola[10b] reported the routine use of the bone marrow in three hundred and twenty-six infusions given to infants. Rooney[10j] gave infusions to infants one hundred and fifty times and reported some complications.

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10. (*a*) Arbeiter, H. J., and Greengard, J.: Tibial Bone Marrow Infusions in Infancy, J. Pediat. **25**:1 (July) 1944. (*b*) Meola, F.: Bone Marrow Infusions as a Routine Procedure in Children, ibid. **25**:13 (July) 1944. (*c*) Bielstein, C. M.: Intramedullary Transfusions in Infants, J. Oklahoma M. A. **37**:243 (June) 1944. (*d*) Herrell, W. E., and Kennedy, R. L. J.: Penicillin: Its Use in Pediatrics, J. Pediat. **25**:505 (Dec.) 1944. (*e*) Gimson, J. D.: Bone Marrow Transfusion in Infants and Children, Brit. M. J. **1**:748 (June 3) 1944. (*f*) Reisman, H. A., and Tainsky, I. A.: The Bone Marrow as an Alternate Route for Transfusion in Pediatrics, Am. J. Dis. Child. **68**:253 (Oct.) 1944. (*g*) Boines, G. J.: Transfusion Via the Bone Marrow, Delaware State M. J. **14**:28 (Feb.) 1942; Infusions Through the Bone Marrow, ibid. **17**:22 (Feb.) 1945. (*h*) Logan, G. B.: Acute Nonsurgical Emergencies Related to the Gastro Intestinal Tract, M. Clin. North America **29**:878 (July) 1945. (*i*) Ravitch, M. M.: Suppurative Anterior Mediastinitis in an Infant Following Intrasternal Blood Transfusion: Operation and Recovery, Arch. Surg. **47**:250 (Sept.) 1943. (*j*) Rooney, E. F.: Bone Marrow Infusion with Two Cases of Localized Osteomyelitis, Arch. Pediat. **61**:611 (Dec.) 1944. (*k*) Dardinski, V. J.: Sternal Transfusion in Infants: Reports of a Fatal Case, M. Ann. District of Columbia **14**:206 (May) 1945. (*l*) Tocantins, L. M., and O'Neill, J. F.: Complications of Intraosseous Therapy, Ann. Surg. **122**:266 (Aug.) 1945. Tocantins, O'Neill and Jones.[6e]

The methods of bone marrow infusion have not been accepted enthusiastically by pediatricians. This may be because indications for its use are rare when cases are handled by physicians who have become proficient in the care of infants and children. Another possible factor may be related to the use of the method by inexperienced personnel. In the hands of such persons the probabilities of poor results and complications are increased. On the other hand, numerous reasons have been given for using the intraosseous method. In cases of peripheral circulatory collapse there is uniform agreement [11] concerning the value of this technic. In situations in which all available veins are thrombosed (through repeated punctures of the vein or burns) this method is a logical substitute for the intravenous route.[12] In the transportation of patients [13] when considerable moving is contemplated, marrow infusion has been suggested. When rapid forceful injections are necessary the intraosseous method may be used.[9k] The value of marrow infusion for uncooperative, irrational infants and children, who are rapidly going into shock or convulsion, is well recognized. Such patients can be given fluids by this method. It has also been recommended in situations in which veins are inaccessible, as with edema, obesity and marasmus. The use of an intraosseous method was felt to be of value in an epidemic of diarrhea of the newborn. For battle casualties it has proved a life-saving measure.[9u-f]

TECHNIC OF BONE MARROW TRANSFUSION

The principle and the technic of this method have been described in previous publications,[9l-m] but for the sake of completeness they are included. The outer splitting needle and stylet are forced through the skin until the bone is reached. The stylet is replaced by the trephine needle, whose cone-shaped, saw-toothed tip (when rotated against the bone) cuts a smooth round opening through the outer laminated bone into the marrow cavity and extracts the bone particles as a core. The outer needle is forced through the smaller opening made with the trephine needle a measured distance into the marrow cavity. This spreads the trephine hole and forms a snugly clasping bony ring, which prevents leakage around the outer needle. The extraction of the core minimizes the possibility of particles of bone plugging the needle and communicating marrow sinusoids.

The needle is made in two sizes. The tibia needle (fig. 1 *A*) is 15 gage and 17 mm. long. This may also be used in the sternum. The

11. Footnotes 9 and 10.

12. Macht.[7a] Soutter.[9e] Arbeiter and Greengard.[10a] Johnston.[9v] Cope and Rhinelander.[9x]

13. Doud and Tysell.[9n] Faxon and Churchill.[9d] Soutter.[9e]

femur needle (fig. 1 *B*) is 15 gage and 37 mm. in length. An adjustable depth control guard is used with this needle. Other instruments and material necessary include a padded footboard (fig. 2), scissors, tape (½ and 1 inch [1.3 and 2.5 cm.]), local anesthetic and antiseptic. A medicine glass containing sterile isotonic solution of sodium chloride, two syringes (one hypodermic and one 10 cc. for aspiration), drapes, rubber gloves, needles for injection of the anesthetic and cotton balls and gauze should also be available. This last-mentioned material may be

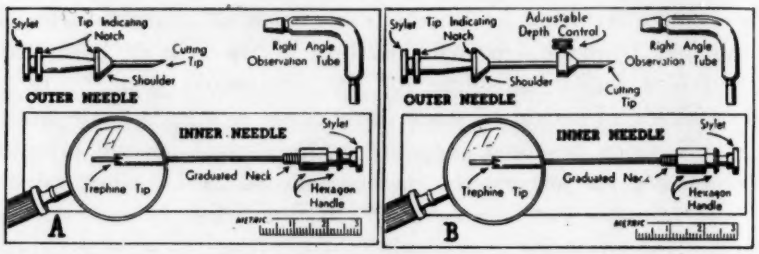

Fig. 1.—Outer splitting needle and stylet and inner trephine needle used in bone marrow transfusions.

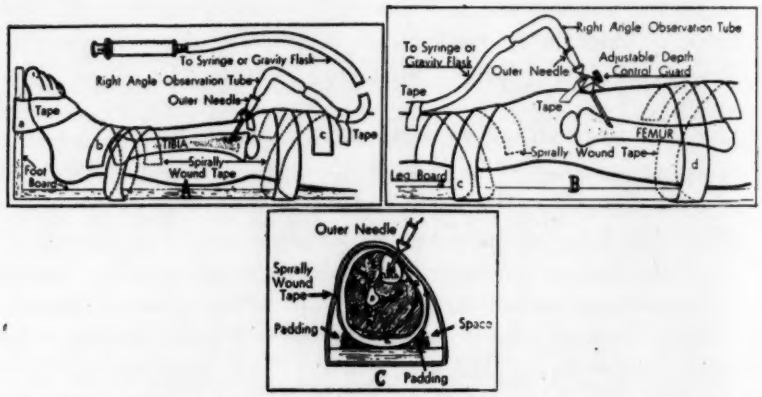

Fig. 2.—An illustration of the procedure followed in preparing the leg and inserting the needles in the tibia and in the femur for bone marrow transfusions.

sterilized as a unit. The infusion set to be used will depend on whether the patient is to receive a slow infusion or a rapid forced injection.

If the tibia is used, the site of puncture is located by palpating the medial flat surface at the proximal end. The tuberosity is felt midway between the medial and the lateral condyles. The point of insertion of the needle is immediately below the tuberosity. The site of puncture in the femur is in the midline and 3 cm. above the external condyle in the lower third of the femur. The bone is firmly grasped in one hand and the needle, directed away from the epiphysial plate, is introduced at

an angle that will allow the bevel to be parallel to the shaft of the bone. It is important that the leg be fixed firmly, and in the process of fixing the leg the venous return should not be impaired. For this reason we recommend spiral taping of the leg and the board (fig. 2, *A* and *B*). If the leg is inadequately immobilized, the needle will become loose and allow fluid to well up under the periosteum and into the subcutaneous tissues. This might result in pressure necrosis. Particular attention should be paid to the possibility of subperiosteal infiltration occurring when forced injections are given. Obviously no fluid should be allowed to enter through the needle without first aspirating the blood-marrow mixture and then injecting isotonic solution of sodium chloride. When the solution is injected, it should be forced in with relative ease. If the solution does not enter the cavity easily, the hollow drill should be reintroduced and rotated to remove possible bone fragments. If fluid then cannot be injected, another bone should be used. When a bone is punctured, it should not be used again for infusion until a firm clot has formed. This usually takes from twelve to twenty-four hours. If a continuous infusion is given, the persons responsible for the immediate care of the patient should be instructed to watch closely for the development of subcutaneous infiltration. If this occurs, the infusion should be stopped.

The intraosseous route is not without danger, and every instance when it is contemplated should represent a definite emergency situation in which the choice of a more conservative route would be impractical. Serious complications have been shown to follow intramedullary infusions, including penetration into the mediastinum (which should not occur in infants and young children), osteomyelitis at the site of infusion, thrombosis of vessels and pressure occlusion of vessels.[14] Frequent references in the literature have mentioned osteomyelitis, osteochondritis, furunculosis, cellulitis, secondarily infected burns, septicemia or bacteremia and infection at the site of injection as contraindications to the intraosseous route. However, the method is recommended as an emergency measure. Frequently the possible complications should be overlooked when the patient's immediate need is fluid therapy. The following case report emphasizes this problem.

REPORT OF A CASE

A 5 day old infant with persistent bile-stained and fecal vomitus was shown to have obstruction to barium at the duodenum. Duodenojejunostomy was done, but the infant continued to vomit and eviscerated on the sixth postoperative day. He had been maintained on parenteral fluids, and all available veins had been

14. Tocantins, O'Neill and Price.[6c] Tocantins.[6h] Papper and Rovenstine.[9b] Papper.[9c] Soutter.[9e] Turkel and Bethell.[9l] Ravitch.[10i] Rooney.[10j] Dardinski.[10k] Tocantins and O'Neill.[10l]

used. Despite the presence of peritonitis and probably of sepsis, a tibial marrow infusion was started and maintained for four days, during which time the peritonitis became worse in spite of antibacterial treatment. On the fourth day subcutaneous infiltration around the puncture site was noted and necrosis of skin and bone rapidly developed. The infusion was then placed in the opposite leg (with another type of needle) but was unsuccessful. A Turkel needle was successfully placed in the distal portion of the femur. The following day the infant died. Autopsy showed a persistent block at the duodenum and generalized peritonitis. The right tibia was cut lengthwise, and extensive osteomyelitis, involving practically all the marrow cavity, was noted.

An attempt to summarize other reported complications can be seen in the table. Several of them were the result of poor judgment as to the best site of infusion or were the result of indiscriminate selection of

Complications Following the Intraosseous Method of Injection Reported in the Literature

Author	Infusions, No.	Complications	No.
Behr [9h]	40+	Osteomyelitis	1
Ellison [9f]	40	None	
Bailey [9i]	60+	Mediastinitis (adult)	1
Ravitch [10i]	1	Mediastinitis (infant)	1
Papper [9c]	?	Subcutaneous abscess	1
		Mediastinitis	1
Arbeiter and Greengard [10a]	43	None	
Meola [10b]	326	Arterial thrombosis	1
Rooney [10j]	100	Osteomyelitis	2
O'Neil, et al.[6j]	116	Mediastinitis (adult)	1
Tocantins, et al.[6k]	79	Osteomyelitis, mentioned in discussion of paper	3
Dardinski [10k]	1	Mediastinitis (newborn infant) (fatal)	1
Reisman and Talnsky [10f]	?	Osteomyelitis	1
Quilligan and Turkel	45	Osteomyelitis (1 reported osteomyelitis, "several" mentioned)	1

cases. Tocatins and O'Neill [10l] have pointed out the analogy between the present status of intraosseous injections and the status of the now commonly accepted methods of infusion ten to twenty years ago. At that time numerous complications to ordinary intravenous injections were reported. Even now, when venous "cut-down" procedures are continued for several days, complications often occur.

The table shows the difficulty of accurately judging the ill effects of the intraosseous method. Frequently reports did not include a series of cases. Some complications were mentioned in the body of the paper as being brought to the attention of the author, as in our case; at another hospital secondary osteomyelitic infections developed in children who received bone marrow infusions. One of the reports [6k] included in the discussion at the end of the article 3 cases of osteomyelitis.

Our experience with this method of administering fluid has been satisfactory in those instances in which a definite emergency existed.

In such circumstances only that amount of fluid necessary to restore good circulatory function was given (10 to 15 cc. per pound [454 Gm.]), and the needle was removed. Approximately 40 such procedures were performed without any complications. One child was brought to our attention in whom osteomyelitis developed in another hospital after such a procedure; in this patient the needle was left in place for approximately four hours. Five infants have been given continuous infusions (two days or longer) via the intraosseous route. The previously described patient is one of this group. In no instance in which fluids were given did we encounter difficulty through using the Turkel needle, and in 1 case the substitution of the Turkel needle for one of the puncture type of needles resulted in a successful infusion. The possibility of fat emboli has been frequently mentioned in the discussions of this technic, but to date no cases have come to our attention. However, Wile has shown that with intraosseous administration of neoarsphenamine emboli did develop in rabbits.[7b] If fluids are to be given over a long period, we do not believe that the intraosseous route is best. It may be utilized in situations in which shock is present, but after the initial shock is overcome, the marrow infusion should be discontinued in favor of more conservative routes of fluid administration.

It should be emphasized that "because of the undeveloped sternum, in children under three (3) years of age, only the long bones (tibia, femur) should be used." The frequency of reports of mediastinal complications in infants justifies such emphasis. If the long bones are not too thick, they may be used in children to the age of 5 years. Sternal infusions may be used in patients over 3 years of age.

CONCLUSIONS

1. The use of the bone marrow as an emergency route for the parenteral administration of fluid is advocated.

2. A technic for administration of fluids by the bone marrow route is described.

3. The advantages of this method depend on the type of needle, which employs a trephine rather than a puncture principle of operation.

4. In 1 of 45 patients receiving fluids by this method osteomyelitis developed at the site of infusion.

CONGENITAL MEDIASTINAL CYSTS OF FOREGUT ORIGIN

JACOB L. OLENIK, M.D.
Adjunct Surgeon, Bronx Hospital
AND
JOSEPH W. TANDATNICK, M.D.
Resident in Pathology, Bronx Hospital
NEW YORK

SINCE 1870, when von Wyss [1] first reported a case of mediastinal cyst lined with primitive esophageal mucosa, 74 cases of intrathoracic cysts of foregut origin have been reported in the literature.[2]

The following members of the staff of the Bronx Hospital, furnished us with the material indicated, in the case reported in this paper: Dr. Bernard S. Denzer, Director of the Pediatric Service, the clinical data; Dr. Joseph Felsen, Director of Laboratories and Research, the pathologic reports and microscopic reproductions.

1. von Wyss, H.: Zur Kenntnis des heterologen Flimmercysten, Virchows Arch. f. path. anat. **51**:143, 1870.

2. (*a*) Hennig, C.: Cystis intestinalis, Cystis citra oesophagum bei einem Neugeborenen, Zentralbl. f. Gynäk. **4**:398-399, 1880. (*b*) Roth, M.: Ueber Missbildungen in Bereich des Ductus omphalo-mesentericus, Virchows Arch. f. path. Anat. **86**:371-390, 1881. (*c*) Hebb, R. G.: Perioesophageal Cyst, Tr. Path. Soc. London **49**:88, 1897-1898. (*d*) Staehelin-Burckhardt, A.: Ueber eine mit Magenschleimhaut versehene Cyste des Oesophagus, Arch. f. Verdauungskr. **15**:584-603, 1909. (*e*) Schmincke, A.: Intramesenteriale und intrathorazische Enterokpstombildung, kombiniert mit abnormer Lungenlappung und durch keilwirbel bedingter kongenitaler Skoliose der oberen Hals- und Brustwirbelssäule, Virchows Arch. f. path. Anat. (supp.) **227**:12-27, 1920. (*f*) Buttenwieser, S.: Beitrag zur Kenntnis des Oesophaguscysten beim Neugeborenen, Ztschr. f. Kinderh. **32**:352-355, 1922. (*g*) Mixter, C. G., and Clifford S. H.: Congenital Mediastinal Cysts of Gastrogenic and Bronchogenic Origin, Ann. Surg. **90**:714-729, 1929. (*h*) Entz, B., and Orosz, D.: Ueber die intrathorakalen Zystenbildungen, Frankfurt. Ztschr. f. Path. **40**:229-246, 1930. (*i*) Fischer, W.: Ueber eine Cyste in der rechten Pleurahöhle, Virchows Arch. f. path. Anat. **275**:711-716, 1930. (*j*) Smith, R. E.: A Case of Mediastinal Dermoid Cyst in an Infant, Guy's Hosp. Rep. **80**:466-469, 1930. (*k*) Poncher, H. G., and Milles, G.: Cysts and Diverticula of Intestinal Origin, Am. J. Dis. Child. **45**:1064-1078 (May) 1933. (*l*) Patterson, E. J.: Congenital Cyst of the Esophagus: Report of Case, Ann. Otol., Rhin. & Laryng. **43**:884-886, 1934. (*m*) Stoeckel, K. H.: Ueber einen Fall von intrathorakaler Enterodermcyste im Mediastinum posterius bei einem Neugeborenen, Zentralbl. f. Gynäk. **59**:2178-2183, 1935. (*n*) Black, R. A., and Benjamin, E. L.: Enterogenous Abnormalities: Cysts and Diverticula, Am. J. Dis. Child. **51**:1126-1137 (May) 1936. (*o*) Brass, K.: Ueber einen Fall von intrathorakalem Enterocystom zugleich ein Beitrag zur Pathogenese,

(Footnote continued on next page)

Of these 35 cysts were lined with epithelium derived from the primitive foregut in the region of the lung bud or from the lung bud itself, 12 cysts were lined with primitive esophageal epithelium,[3] 15 with gastric mucosa, 4 with intestinal mucosa and 8 with mixed types of esophageal, gastric, enteric and respiratory epithelium. The 8 cysts last mentioned include 4 lined with gastroenteric epithelium, 2 with esophagogastric lining, 1 with esophagotracheal mucosa and 1 with bronchoesophageal epithelium.

The comparative rarity of these cysts, especially those lined with gastroenteric epithelium, prompts us to report the following case:

REPORT OF A CASE

History.—Baby D. J. L., a 9 day old, white boy was transferred from the nursery to the pediatric service (Bronx Hospital, New York) because of several attacks of dyspnea, rapid breathing and cyanosis occurring sporadically during the previous two days.

Family History: The mother was 28 years old and in good health; she had one other child, 4 years of age, who was well and had no congenital abnormalities. The father was 33 years of age and in good health.

Previous History: The infant was spontaneously delivered after a full term pregnancy. The birth weight was 6 pounds and 12 ounces (3,267 Gm.). Physical examination the day after birth revealed no abnormalities. The infant nursed poorly and failed to gain any weight. On the seventh day he had three attacks of rapid breathing and dyspnea together with cyanosis. The cyanosis

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Frankfurt. Ztschr. f. Path. **50**:26-33, 1936. (*p*) Böss, C.: Kongenitale, mit Magenschleimhaut ausgekleidete Mediastinalcyste mit in die Lunge penetrierendem chronischem Ulcus pepticum, Virchows Arch. f. path. Anat. **300**:166-179, 1937. (*q*) Ladd, W. E.: Duplications of the Alimentary Tract, South. M. J. **30**: 363-371, 1937. (*r*) Guillery, H.: Eine Wirbelsäule eingewachsen mediastinale Zyste (Vorderdarmzyste), Zentralbl. f. allg. Path. u. path. Anat. **69**:49-53, 1937. (*s*) Seydl, G. N.: Eine kongenitale Magenwandcyste im Mediastinalraum mit in die Lunge perforiertem Ulcus pepticum, Frankfurt. Ztschr. f. Path. **52**:346-354, 1938. (*t*) Ladd, W. E., and Gross, R. E.: Surgical Treatment of Duplications of the Alimentary Tract, Surg., Gynec. & Obst. **70**:295-307, 1940. (*u*) Nicholls, M. F.: Intrathoracic Cyst of Intestinal Structure, Brit. J. Surg. **28**:137-143, 1940. (*v*) Carlson, H. A.: Congenital Cysts of the Mediastinum, J. Thoracic Surg. **12**:376-393, 1943. (*w*) Wyllie, W. G., and Pilcher, R. S.: Intrathoracic Cysts of Intestinal and Bronchial Structure, Arch. Dis. Childhood **18**:34-40, 1943. (*x*) Olken, H. G.: Congenital Gastroenteric Cysts of the Mediastinum: A Review and Report of a Case, Am. J. Path. **20**:997-1009, 1944. (*y*) Ladd, W. E., and Scott, H. W., Jr.: Esophageal Duplications or Mediastinal Cysts of Enteric Origin, Surgery **16**:815-835, 1944. (*z*) Laipply, T. C.: Cysts and Cystic Tumors of the Mediastinum, Arch. Path. **39**:153-161 (March) 1945. (*a'*) Adams, W. E., and Thornton, T. F., Jr.: Bronchogenic Cysts of the Mediastinum, J. Thoracic Surg. **12**:503-516, 1943. (*b'*) Von Wyss.[1]

3. Esophageal cysts are commonly not reported as mediastinal cysts. However, by their location immediately adjoining or actually within the wall of the esophagus, itself a mediastinal structure, they should be so considered.

lasted from five to ten minutes, while the dyspnea lasted about forty-five minutes. Between these paroxysms the child appeared well. On the ninth day after another of these attacks he was transferred to the pediatric service.

Physical Examination and Clinical Course.—Physical examination revealed a fairly well nourished, white boy, who was dyspneic and breathing rapidly. No abnormal physical conditions were found to account for the symptoms. He was placed in an oxygen tent. Thereafter, whenever he was taken out of the tent cyanosis and dyspnea developed.

Three days after transfer roentgenologic examination of the chest revealed massive atelectasis of the lungs with obstructive emphysema at the bases. There were also several hemivertebrae in the dorsal region of the spine (fig. 1). Physical examination at this time showed the absence of breath sounds at both pulmonary bases, more pronounced on the left side.

Fig. 1.—Roentgenogram of the chest showing pronounced atelectasis of the lungs with obstructive emphysema at the bases. There are also several hemivertebrae in the dorsal region of the spinal column. The cyst did not visualize on roentgen examination.

Episodes of dyspnea and cyanosis now occurred frequently in spite of continuous administration of oxygen. On the seventh day after transfer another attack of cyanosis and dyspnea occurred, with a respiration rate, however, of 10 per minute. In spite of the administration of various respiratory stimulants the baby failed to improve and died nine hours after the onset of this last episode.

Laboratory Data.—The urine was normal except for a trace of albumin. The blood count showed a hemoglobin content of 118 per cent (17 Gm.), 5,710,000 red blood cells and 14,850 white blood cells, with 63 per cent neutrophils and 37 per cent lymphocytes.

Postmortem Report.—The following is the gross description (only the essential pathologic observations are given here.). The body was that of a white boy weighing 6 pounds and six ounces (2,920 Gm.) and measuring 20 inches (50 cm.) in length. The face was cyanotic. The spleen, the kidneys

and the right lung were congested. The left lung was completely atelectatic and also showed congestion of the lower lobe.

The left thoracic cavity was half filled by a tense, cystic, oval mass measuring 7 by 3.5 by 3 cm. The mass was behind the left lung. The cyst was thin walled and loosely attached to the side of the vertebral column from the fourth

Fig. 2.—Section of the cyst wall showing mucosa with typical simple columnar epithelium (*A*), a submucosa without lymph nodules (*B*) and a muscular coat consisting of a layer of inner circular (*C*) and a layer of outer longitudinal muscle (*D*). There is also a serosa (*E*) present. This may, however, be the pleura covering the cyst. This section resembles intestinal wall.

to the ninth thoracic vertebra and to the adjoining ribs. It was firmly anchored, however, to the side of the body of the fourth thoracic vertebra. The cyst was found to contain a clear, straw-colored, watery fluid.

Microscopic Examination: Right Kidney. There was a pronounced cloudy swelling of the tubular epithelium, obliterating the lumens in most cases. The renal vessels were congested.

Lungs. In the right lung the air vesicles were fairly well distended. Some contained fluid. The pulmonary vessels were congested. There were localized

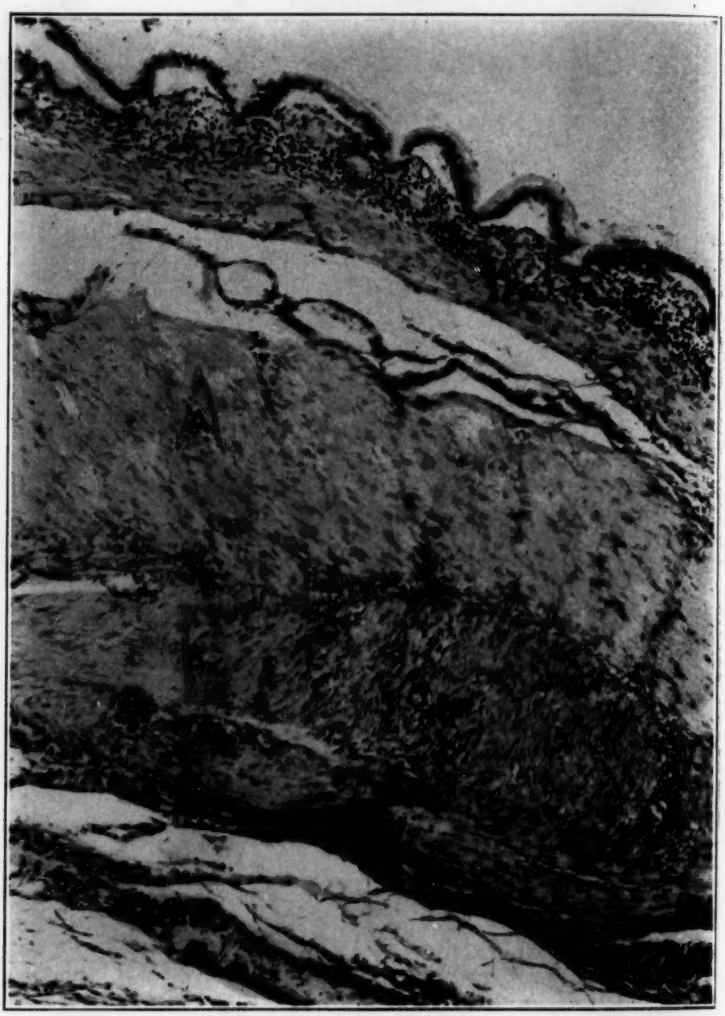

Fig. 3.—Another section of the cyst wall showing mucosa and submucosa similar to that shown in figure 2. The muscular coat, however, is composed of three distinct layers (*A*, *B* and *C*). There is also a serosal layer present, external to the muscular coat. This section resembles stomach wall.

areas of compensatory emphysema and some perivascular areas of granular, brown pigment deposition. The left lung was almost completely atelectatic. There were scattered punctate areas of granular, brown pigmented deposition.

The bronchial branchings were filled with cellular material, chiefly polymorphonuclear cells.

Cyst Wall. One section resembled the intestinal wall (fig. 2), the structure being well defined. There was a mucosa with typical simple columnar epithelium, a submucosa without lymph nodules and a muscular coat consisting of a layer of inner circular and a layer of outer longitudinal muscle. There was also a serosa present. This, however, might have been the pleura covering the cyst. In this and other sections the mucosa contained goblet cells or goblet-like cells of the simple columnar type and varied as to the depth and number of glands present. Another section resembled stomach wall (fig. 3). There were mucosa and submucosa similar to that in the other sections. The muscular coat, however, was composed of three distinct layers.

COMMENT

Embryology and Nomenclature.—Various explanations of the origin of congenital mediastinal cysts have appeared in the literature. Among the more popular concepts are: (1) the twinning theory, (2) the diverticulum theory of Lewis and Thyng,[4] who have stated the belief that diverticula-like projections occurring along the gastrointestinal tract of the embryo are pinched off and carried away to develop as cysts, and (3) the vacuolation theory of Keith.[5] The explanation for the difference in the mucosal elements of the lining of the cysts and of the lining of the portions of the gastrointestinal tract from which the émigreé cells are supposed to have arisen is that metaplastia occurred.

Our concept is that all the cysts are derived from the foregut at or near the region of the lung buds. In this small area the cells that are predestined to become the various constituents of the different sections of the gastrointestinal and respiratory tracts are rapidly developing and multiplying in close proximity to each other. Single cells or small groups of similar or dissimilar cells are desquamated or pinched off from this complex anlage and are carried away to develop separately, later becoming cysts. The descent of the pericardium and the natural lengthening of the gastrointestinal tract plus the development and growth of the respiratory tract are partly responsible for the migration and final position of these cells.

In esophageal cysts separation of cells probably occurs at a more advanced stage; hence migration is not so pronounced, the cysts developing close to their source of origin, often within the wall of the esophagus itself.

The separation of the cells that form bronchogenic cysts may occur early or may not take place until after the lung buds have developed.

4. Lewis, F. T., and Thyng, F. W.: The Regular Occurrence of Intestinal Diverticula in the Embryos of the Pig, Rabbit and Man, Am. J. Anat. **7**:505, 1907.

5. Keith, A.: Human Embryology and Morphology, Baltimore, William Wood & Company, 1933.

Grossly all the cysts in our discussion resemble one another, their classification depending on the histology of the lining mucosa and wall. This, in turn, depends on the portion of the primitive foregut from which the aberrant cells have become separated.

If the tissue strayed from the foregut in the region of the lung bud or from the lung bud itself, the resulting cyst would be lined with respiratory epithelium. The special term ("bronchogenic cyst") is used in the literature to denote this type of mediastinal cyst. It has also been referred to as "accessory lung." The cavity of these cysts does not communicate with that of the bronchial tree. Bronchogenic cysts are lined with ciliated columnar epithelium, the cells often resembling primitive esophagus. The mucosa contains secreting glands, and the submucosa frequently has cartilage in it. The wall also has smooth muscle.

If the cysts have developed from tissue that sprang from the regions of the foregut that give rise to esophagus, stomach or intestines, they will be lined, respectively, with esophageal, gastric or enteric epithelium. Their walls will resemble those of the normal adult structures.

Mixed cysts referred to in the opening paragraph of this paper are the results of the development of groups of dissimilar cells derived from borderline areas of the primitive foregut and are classified in accordance with the component elements in their lining walls. Thus there are bronchoesophageal, esophagotracheal, esophagogastric and gastroenteric cysts. Other combinations. of course, are possible.

Review of the Literature.—The totals of the various types of mediastinal cysts of foregut origin reported to date were given in the opening paragraph of this article.

Thirty-five cases of bronchogenic mediastinal cysts have been reported thus far and were recently reviewed by Laipply.[2z] In 19 of these the cysts occurred in males, and in 14 in females; in 2 cases no sex was given. Thirteen of the patients were not over 9 years of age. Six were operated on, with 4 cures and 2 deaths. Bronchogenic mediastinal cysts are most commonly found in the posterior part of the superior mediastinum.

A study of the 39 cases of esophageal, gastric, enteric and mixed mediastinal cysts reveals the following facts:

In all but 5 cases the cysts were single and unilocular; in 3 they were bilocular and in 1 multilocular,[2b] while in 1 case two gastric mediastinal cysts were found.[2k] Twenty-six of the patients were males, and 10 were females. In 3 cases no sex was mentioned.

It would seem that esophageal cysts are compatible with life and good health, since 7 of the 12 patients in whom they were found were adults and 5 were children. The small size and less vulnerable position of these cysts are the likely explanation for this. Of the remaining

27 subjects in this group, 1 was stillborn and 5 lived only a few hours after delivery. The oldest patient was 3 years and 9 months old. The only exception was the case reported by Adams and Thornton [2a'] of a bronchoesophageal cyst in a 54 year old man.

The largest cyst was enteric and measured 14 by 6.5 cm.[2n] The smallest cyst was of the esophageal type and was 13 mm. in diameter.[2d]

The usual location for the cysts in this group is the posterior mediastinum, and, in the cases of the esophageal cysts, close to or within the wall of the mediastinal portion of the esophagus. Of the 39 esophageal, gastric, enteric and mixed mediastinal cysts, 22 were found in the right and 14 in the left hemithorax. In 3 of the cases, the cysts were in the midline.

The contents of the cysts varied in consistency from watery to gelatinous and in color from gray to green. Occasionally the contents were blood tinged. In some cases the contents were acid in reaction and contained pepsin.

In 1 patient with a gastric type of cyst,[2p] there was present a peptic ulcer in the cyst wall. The ulcer had perforated into the lower lobe of the right lung. Excision of the cyst was attempted, but the patient died during the operation. In another case of gastric cyst with a peptic ulcer in its wall,[2s] the ulcer had perforated into the right lung, the patient dying of hemorrhage.

Sixteen of the 39 patients were treated surgically. Eight recovered completely, and 8 died postoperatively.

Congenital anomalies of many varieties, including spina bifida, talipes, diverticula of the intestine, scoliosis, patent foramen ovale and hydrocephalus, were found in 18 of the 39 cases in the last group discussed.

Symptomatology.—The symptoms produced by mediastinal cysts of primitive foregut origin, like those produced by other types of intrathoracic cysts, are primarily the results of mechanical pressure on the adjoining structures. They therefore vary with the location, size, consistency and the rate of growth of the cyst. These symptoms may be present at birth or may appear soon thereafter. In some cases, however, symptoms do not appear for several years, while in others symptoms never occur. This is especially true of esophageal cysts.

The lungs and bronchi are the structures most often embarrassed. Frequently the heart is displaced to one side. Thus, the usual symptoms are dyspnea, cyanosis, cough and hemoptysis. Compression of the esophagus may cause dysphagia and even hematemesis. Pain, if present, may be due to extrinsic pressure on nerves or to intracystic pressure. The occasional presence of peptic ulceration in these cysts may also be a source of pain.

In the cases reported in the literature, the symptoms were most often continuous and unrelenting, but in 7 of the cases (including

our own) they appeared in recurrent attacks, between which the patients were fairly comfortable. These alternations of symptoms might be partly due to changes in the size of the cyst caused by increased secretion with distention of the cyst at one time and absorption of the secretion at another time. The former might be due to reflex activation of the secreting glands resulting from smell, taste or ingestion of foods.

In this connection it is interesting to speculate on whether the parenteral administration of a small quantity of histamine to the patient would increase the amount of secretion into a gastroenteric cyst so that a change in the size of its roentgenologic shadow could be visualized.

Diagnosis.—Diagnosis is difficult. Newborn infants suffering from dyspnea, cyanosis, cough and other signs and symptoms are most often the victims of mucous plugs which block part of the bronchial tree. Patients with congenital cardiac anomalies may also exhibit these symptoms. Congenital intrathoracic cysts, although of rare occurrence, must be borne in mind when the conditions just mentioned have been ruled out. Roentgenologic examination usually suggests the diagnosis, but occasionally even this modality fails. As in our case, the roentgenograms may show only atelectasis, or an all-concealing pleural effusion may obscure the underlying cyst. When a posterior mediastinal mass is demonstrated by roentgenologic examination, one may suspect the diagnosis of mediastinal cyst. The further differentiation between these cysts and other tumors and cysts occurring in the posterior mediastinum can rarely be made before exploration. Symptomless cysts are occasionally discovered by roentgenologic studies made for unrelated conditions. Most often, however, they are found during postmortem examination.

In studying the size and location of gastric, enteric and gastroenteric cysts reported on in the literature, whose dimensions and locations are specifically given, it is seen that an aspirating needle introduced on the affected side just lateral to the body of the fourth thoracic vertebra below its transverse process would have entered all of them. Aspiration would therefore seem to be an additional method of arriving at a diagnosis. If fluid is found, it can be aspirated and the cavity refilled with a radiopaque substance. Roentgenologic examination would then outline the limits of the cyst. It must be borne in mind that with this procedure the needle might pass through the free pleural cavity in some of the cases. If a small bore needle is used, the leakage that might possibly occur from the cyst into the pleural space will be minimized.

Treatment.—After a diagnosis of intrathoracic cyst has been arrived at, surgical intervention should be considered. Frequent aspiration might be sufficient to keep the child symptom free until it is in better physical condition to withstand operation. Of course, there is always

the danger of infection in the use of such a method, but the risk is not prohibitive, especially if administration of penicillin and chemotherapy are utilized. When the patient is finally operated on, the chance for recovery is considerable. Laipply [2z] found in the literature 4 recoveries in the 6 cases in which operations were performed for the removal of the bronchogenic type of cysts of the mediastinum. We found cause for even greater encouragement while studying the results in the 16 reported cases in which there were operations for the remaining varieties of mediastinal cysts of foregut origin, i.e., the esophageal, the gastric, the enteric and the mixed.

The first operative removal of a mediastinal cyst of the latter-named varieties was accomplished by Kraus, according to the report by Buttenwieser [2f] in 1922; the patient survived the operation. Mixter and Clifford [2g] in 1929 reported 2 cases in which there were operations, with one recovery. In the following ten years there were reported in the literature 4 cases in which operations were performed. all with fatal results: 2 by Entz and Orosz [2h] and 1 each by Poncher and Milles,[2k] and Böss.[2p] During this time also, Smith [2j] and Fischer [2l] reported 1 case each in which fatalities ensued in spite of tapping the cysts. From 1940 to the present date, 7 additional cases of operative treatment have been reported, 1 each by Nicholls,[2u] Carlson,[2v] Wyllie and Pilcher [2w] and Adams and Thornton,[2a'] all patients surviving; and 3 by Ladd and Scott,[2y] 2 of whose patients recovered.

It is seen that, though the mortality rate in this group of 16 cases in which operative intervention was attempted is 50 per cent, the preponderance of deaths occurred in the cases in which operation was performed before 1940 and that in 6 of the 7 cases in which operation was performed after 1940 the patients survived.

The great strides made in the practice of preoperative and postoperative care, more skilful induction of general anesthesia and better operative technic undoubtedly account for the tremendous improvement in the results of the last five years.

The type of operation most often used was an attempt to excise the cyst completely in one stage, and when that failed because of the intimate attachment of the cyst to the esophagus marsupialization and subsequent destruction of the mucosal lining by packing, chemicals or curettage were resorted to in the latter cases; it was occasionally found necessary to attempt complete excision at a later date.

SUMMARY

A case of gastroenteric cyst of the mediastinum in a newborn infant has been presented.

The literature on congenital mediastinal cysts of foregut origin has been reviewed. Since 1870, 74 cases (including our own) with

these types of intrathoracic cysts have been reported. In 35 the cysts were lined with respiratory epithelium; in 12, with primitive esophageal epithelium; in 15, with gastric mucosa; in 4, with intestinal mucosa, and in 8, with mixed types of esophageal, gastric, enteric and respiratory epithelium.

We believe all these cysts to have a common origin in the primitive foregut. The classification of the cysts depends on the histologic structure of their mucosal lining and wall.

The symptoms produced by these cysts are due to pressure on the adjoining thoracic structures. The commonest are dyspnea, cyanosis and cough. They usually appear soon after birth. In our case, as in 6 others reported in the literature, symptoms alternated with periods of comparative comfort.

Diagnosis is difficult because several other conditions lead to similar symptoms. When intrathoracic cysts are suspected, careful roentgenologic examination may be helpful. However, roentgenologic examination may fail to outline the cysts. Aspiration of the cyst and introduction of a radiopaque substance into the cavity should be attempted.

Treatment of these cysts is always surgical.

SCARLET FEVER AMONG PUEBLO INDIANS

Observations on Susceptibility and Occurrence

M. L. FRANK, M.D.
Senior Physician, Indian General Hospital
AND
C. A. ELKIN, B.S.
Hospital Technician, Indian General Hospital
ALBUQUERQUE, N. MEX.

IT is the purpose of this communication to show that Pueblo Indians are as susceptible to scarlet fever as are non-Indians if the Dick test is used as the criterion of susceptibility and to show by the presentation of a number of clinical cases of scarlet fever among fullblooded Pueblo Indians that the disease is actually contracted by susceptible Indians.

Previous investigators have suggested that scarlet fever is an uncommon disease among the Indians of the Southwest. Hrdlička,[1] in 1908, was the first to observe that scarlet fever was rarely found among Southwestern Indians. R. J. Stroud,[2] United States Indian Service physician at Salt River Agency in 1925, tested a series of fullblood Indian children and a group of Mexican children between the ages of 6 and 13 years with the Dick test and found 40 per cent positive reactors in each group. He concluded that Indians could succumb to scarlet fever, although he had been told that they were immune.

After Hrdlička's study, no further publications dealing with the subject of scarlet fever among Indians appeared until 1926, when Sherwood, Nigg and Baumgartner[3] made a comparison of the results of skin sensitivity tests for scarlet fever performed on Indians with the results of tests done on white persons having a history of scarlet fever. They assumed that the Indians had a racial immunity to the

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From the Medical Service, United Pueblos Agency, United States Indian Service.

1. Hrdlička, A.: Physiological and Medical Observations Among the Indians of Southwestern United States and Northern Mexico, Bulletin 34, Smithsonian Institute, Bureau of American Ethnology, 1908, p. 190.

2. Stroud, R. J.: Personal communication to the authors.

3. Sherwood, N. P.; Nigg, C., and Baumgartner, L.: Studies on the Dick Test and Natural Immunity to Scarlet Fever Among American Indians, J. Immunol. **11**:343 (May) 1926.

disease and based their assumption on Hrdlička's work on the results of their tests and on a series of questionnaires sent to eighty-four Indian Service physicians. Sixty-six of these physicians stated that they had never seen a case of scarlet fever among fullblood Indians, even when epidemics occurred among the white population near the reservation. The other eighteen had seen a few or doubtful cases. However, in the same survey, about 40 per cent of a group of sixteen physicians who had been in the Indian Service more than ten years stated that they had never seen a case of diphtheria, a disease which was not considered to be uncommon among nonimmunized Southwestern Indians.

In studying scarlet fever, Sherwood and his associates at Haskell Institute, Lawrence, Kan., performed cutaneous sensitivity tests, using Zingher's toxin, on 324 fullblood Indian students whose ages ranged from 5 to 20 years. They obtained an average of 17.2 per cent positive reactions, ranging from 72.7 per cent in the 5 to 10 year group to 8.8 per cent in the 20 year group. The conclusion drawn from this survey was that even though many Indians had a cutaneous sensitivity to scarlet fever toxin, and so would seem to be susceptible to scarlet fever, there was some local tissue mechanism present, developing in the course of the illness, which protected them against the disease.

In the autumn of 1944, when numerous cases of scarlet fever existed among the white population of the Albuquerque area, it was decided to investigate again the possibility that scarlet fever might occur among Indians and to recheck their susceptibility to the disease by means of the Dick tests. It is believed that the closer contact between the Indian Service personnel and the Indian population which has been established in the last twenty years due to increased transportation facilities and to increased cooperation of the Indians themselves, may well give more complete information than the previous investigators have been able to obtain.

In this investigation Dick tests were performed on 750 Pueblo and 66 Navajo Indian children, approximately 90 per cent of whom were fullblood (the other 10 per cent having a possible small percentage of white blood), and on a control group of 236 children of an Anglo-Spanish country school located near Albuquerque. All syringes and needles were new and were sterilized by autoclaving. Injections of 0.1 cc. of Dick toxin (Parke, Davis & Company) were made intradermally on the flexor surface of the forearm and observed in twenty to twenty-four hours. All vials of toxin which had been partially used were discarded at the end of the day to avoid contamination and the possibility of false reactions. The ages of the Indian children ranged from 5 to 18 years and the ages of the Anglo-Spanish group from 8 to 14 years.

It was found that 22 per cent of the 816 Indian children tested had positive reactions to the Dick test, as compared with 14 per cent positive reactions among the 236 Anglo-Spanish children tested. In the Indian group we obtained an average of 27 per cent positive reactions among the 304 children in the age group of 5 to 11 years and an average of 20 per cent positive reactions among the 512 children in the age group of 12 to 18 years. These results are similar enough to those for the Anglo-Spanish group to state that the two groups have comparable reactions to the Dick test. It has been observed that the higher the age of the children given the Dick test, the lower the percentage of positive reactions. It is also possible that the percentage of positive reactions may vary depending on the region of the country in which the children are tested. Peacock, Bigler and Werner [4] at the children's Memorial Hospital in Chicago performed Dick tests on a group of children routinely admitted whose ages ranged from 6 to 12 years. They found approximately 37 per cent of positive reactions, the percentage varying in decreasing incidence from 48 per cent positive in the 6 year group to 28 per cent positive in the 12 year group.

Dick tests performed by Pevaroff and Hindman [5] in Cleveland among white children in the 5 to 9 age group elicited 57.3 per cent positive reactions; in the 10 to 14 age group, 27.5 per cent positive reactions, and in the 15 to 19 age group, 16.7 per cent positive reactions. Results of the Dick tests on Negro children in the same age groups did not vary significantly from the percentage of positive reactions of the Dick test obtained in white children.

Eight cases of clinical scarlet fever were observed in the Laguna area (New Mexico) from April to September 1945. In all cases there was a typical clinical picture of scarlet fever, with headache, pharyngitis, glossitis, pyrexia and generalized erythema characterized by a fine punctate eruption. The erythema faded on pressure; Pastia's lines were noted. There was a varying degree of desquamation of the hands, feet and body, starting about a week after the onset of the symptoms. All these symptoms appeared in varying grades of intensity.

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4. Peacock, S.; Bigler, J. A., and Werner, M.: Scarlet Fever, Hemolytic Streptococci Cultures and Dick Tests in a Children's Hospital, Am. J. Dis. Child. **57**:759 (April) 1939.

5. Pevaroff, H. H., and Hindman, S. M.: The Dick Test in White and Negro Children Resident in a Congested Section of Cleveland, Am. J. Hyg. **19**:749 (May) 1934.

The following case histories are presented to support a conviction that scarlet fever exists among fullblood Indians. The fact that in 3 of the cases in which Dick tests were routinely performed in November and December 1944 the reactions were positive prior to the contraction of clinical scarlet fever and negative immediately after the disease is to us striking evidence of the existence of scarlet fever among Indians. Unfortunately, the other 5 cases were not included in this initial study and Dick tests had not been given prior to contraction of the disease.

REPORT OF CASES

CASE 1.—R. S., a fullblood Indian girl, aged 9 years, had clinical symptoms of scarlet fever. On culture of materials from the throat, beta hemolytic streptococci of Lancefield group A were isolated. The reaction to the Dick test was positive prior to and negative after the illness.

CASE 2.—E. M., a fullblood Indian boy, 5 years old, had clinical symptoms of scarlet fever. Culture of materials from the throat yielded beta hemolytic streptococci of Lancefield group A. A Dick test performed after the illness elicited a negative reaction.

CASE 3.—W. R., a fullblood Indian boy, aged 7 years, had clinical symptoms of scarlet fever. Beta hemolytic streptococci of Lancefield group A were isolated on culture of materials from the throat. A Dick test performed after the illness elicited a negative reaction. This patient's sister had a sore throat but no rash.

CASE 4.—M. F., a fullblood Indian girl, 4 years old, had clinical symptoms of scarlet fever. Culture of materials from the throat yielded beta hemolytic streptococci of Lancefield group A. A Dick test performed after her illness elicited a negative reaction.[6]

CASE 5.—L. F., a fullblood Indian boy, 9 years of age, the brother of M. F., had symptoms of scarlet fever. On culture of materials from the throat, beta hemolytic streptococci of Lancefield group A were isolated. A Dick test performed after the illness elicited a negative reaction.[6]

CASE 6.—M. D., a fullblood Indian boy, 7 years old, had clinical symptoms of scarlet fever.. Culture of materials from the throat yielded beta hemolytic streptococci of Lancefield group A. The reaction to the Dick test was positive prior to and negative after the illness.

CASE 7.—L., a 5 year old fullblood Indian boy, had clinical symptoms of scarlet fever. Culture materials from the throat were lost while being transported to the laboratory. A Dick test, performed after the illness, elicited a negative reaction.

CASE 8.—B. M., a 7 year old boy, who may be one eighth to one sixteenth white, had clinical symptoms of scarlet fever. Culture of material from the

6. These patients were exposed to the disease through a 5 year old child, who came into the area in which they lived from Winslow, Ariz. This child had a sore throat but no evidence of rash. L. F. (case 5) contracted scarlet fever five days after exposure to this child and M. F. (case 4) eight days after exposure..

throat yielded beta hemolytic streptococci of Lancefield group A. The reaction to the Dick test was positive prior to and negative after the illness.

An effort was made to type further the hemolytic streptococci isolated from the throats of these children, but owing to technical difficulties this was impossible.

In conclusion, the results of the Dick tests show a close similarity between the percentage of positive reactions obtained from testing an Indian group and an Anglo-Spanish group in the same area. The fact that scarlet fever is present among Indians has been shown by the discovery of 8 actual cases in one area over a period of five months. The conclusion reached is that closer scrutiny of possible cases of scarlet fever would demonstrate that there are many more instances of this disease in Indians.

Superintendent John Evans, of the United Pueblos Agency, and Miss Alice Touhey, field nurse in the Laguna area, United Pueblos Agency, cooperated with us in this study; Dr. R. B. Snavely, Indian Service Director of Health, gave encouragement, and Dr. M. Pijoan, guidance.

CAUSES OF PREMATURITY

VII. Influence of Uterine Bleeding on the Incidence of Prematurity

ESTELLE W. BROWN, B.S.

ROBERT A. LYON, M.D.
AND
NINA A. ANDERSON, M.D.
CINCINNATI

UTERINE bleeding during pregnancy may be a symptom of various pathologic conditions. A diagnosis of premature separation of the placenta or of placenta previa can be made in some instances, but in others a definite underlying lesion is difficult to ascertain. The incidence of premature delivery is generally elevated among women who suffer from any of the conditions causing uterine bleeding during pregnancy. In 20 previous reports in the literature [1] the incidence of placenta previa varied from 1.3 to 9.0 per cent among the mothers of premature infants; premature separation of the placenta from 0.2 to 5.1 per cent, and bleeding from unstated causes from 1.2 to 18 per cent. In our preliminary study [2] bleeding from undetermined causes was found to occur in a significantly greater number of mothers of premature infants than in those of full term infants. The group of patients with placenta previa or with premature separation of the placenta was too small at that time to justify comparisons.

Available for our present study are the records of 13,329 mothers and infants, and the separate groups of mothers suffering from different types of uterine bleeding are large enough to permit statistical evaluation of the data. Mothers who had no abnormality of pregnancy except bleeding and those who had entirely normal pregnancies have been placed in separate categories. The comparison of prematurity rates among the offspring of these different groups provides information regarding the influence of bleeding on the incidence of prematurity.

From the Children's Hospital Research Foundation and the Department of Pediatrics, University of Cincinnati College of Medicine.

1. Anderson, N. A., and Lyon, R. A.: Causes of Prematurity: I. Review of the Literature, Am. J. Dis. Child. **58**:586 (Sept.) 1939.

2. Anderson, N. A.; Brown, E. W., and Lyon, R. A.: Causes of Prematurity: II. Comparison of Maternal Histories of Premature and of Full Term Infants, Am. J. Dis. Child. **61**:72 (Jan.) 1941.

DEFINITIONS

The definitions of prematurity and of stillbirth employed in this study have been described in a previous report.[3]

Uterine bleeding was considered to be slight if the patient gave a history of occasional spotting, continued menses or the loss of only a small amount of blood early in pregnancy with no definite evidence of placenta previa or of premature separation of the placenta. Slight bleeding occurring within twenty-four hours before delivery was not considered abnormal. The diagnoses of placenta previa and of premature separation of the placenta were usually made with certainty by the obstetrician attending the patient. In some instances the cause of bleeding which occurred late in pregnancy was not apparent. It seemed probable, however, that partial or marginal placenta previa was the most likely etiologic factor, and the patients with this symptom were so classified.

Uterine bleeding associated with trauma occurred in a few instances. Traumatic agents included serious accidents, falls and blows. It was impossible to obtain an accurate estimate of the incidence of criminal induction of labor. Since the mothers with abortions were not included in this study, it is probable that uterine trauma due to criminal induction of labor in the group under consideration was relatively infrequent.

RESULTS

Mothers with Symptoms of Uterine Bleeding.—Among the entire group of 7,357 white women, 933, or 13 per cent, had some form of uterine bleeding. The incidence of prematurity among the offspring of the group of women who had no uterine bleeding was 7 per cent. When slight bleeding occurred (573 patients), the incidence of premature delivery rose to 14 per cent, a difference of statistical significance. Placenta previa occurred in 240 instances, and the rate of prematurity among the offspring of this series was 30 per cent, again a significant difference. For a relatively few patients (94) a definite diagnosis of premature separation of the placenta was made, and in this group the incidence of premature delivery was 53 per cent. Bleeding associated with trauma occurred in 26 patients and was followed by premature delivery in 27 per cent of the group (table 1).

In the Negro women uterine bleeding of all types occurred less frequently than in the white. A total number of 607, or 10 per cent, of the entire group of Negro women had such symptoms during pregnancy as compared with 13 per cent of the group of white women, a difference of statistical significance. However, the rate of premature delivery among these groups was essentially the same in the two races. The incidence of prematurity among the offspring of mothers who had no symptoms of bleeding was 11 per cent. Slight uterine bleeding was accompanied with premature delivery in 19 per cent of the patients,

3. Brown, E. W.; Lyon, R. A., and Anderson, N. A.: Causes of Prematurity: IV. The Influence of Maternal Illness on the Incidence of Prematurity; Employment of a New Criterion of Prematurity for the Negro Race, Am. J. Dis. Child. 70:314 (Nov.-Dec.) 1945.

while placenta previa and premature separation of the placenta were associated with premature birth rates of 38 per cent and 48 per cent respectively. Such differences in incidence are unquestionably significant (table 2).

TABLE 1.—*Incidence of Premature Births to Women Who Had Various Types of Abnormal Uterine Bleeding During Pregnancy (Single Births Only)*

	Live-Born			Stillborn			Live-Born and Stillborn		
	Premature	Full Term	Total	Premature	Full Term	Total	Premature	Full Term	Total
White Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)									
Slight bleeding	70 (13%)	489	559	10 (71%)	4	14	80 (14%)	493	573
Placenta previa	56 (26%)	161	217	15 (65%)	8	23	71 (30%)	169	240
Premature separation	39 (48%)	42	81	11 (85%)	2	13	50 (53%)	44	94
Bleeding due to trauma	5 (21%)	19	24	2 (100%)	0	2	7 (27%)	19	26
Total bleeding	170 (24%)	711	881	38 (73%)	14	52	208 (22%)	725	933
No bleeding	398 (6%)	5,923	6,321	62 (60%)	41	103	460 (7%)	5,964	6,424
Total number of patients	568 (8%)	6,634	7,202	100 (65%)	55	155	668 (9%)	6,689	7,357
Negro Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)									
Slight bleeding	68 (19%)	297	365	3 (75%)	1	4	71 (19%)	298	369
Placenta previa	41 (30%)	95	136	21 (75%)	7	28	62 (38%)	102	164
Premature separation	16 (38%)	26	42	15 (68%)	7	22	31 (48%)	33	64
Bleeding due to trauma	2 (20%)	8	10	0	0	0	2 (20%)	8	10
Total bleeding	127 (23%)	426	553	39 (72%)	15	54	166 (27%)	441	607
No bleeding	541 (10%)	4,677	5,218	71 (48%)	76	147	612 (11%)	4,753	5,365
Total number of patients	668 (12%)	5,103	5,771	110 (55%)	91	201	778 (13%)	5,194	5,972
Negro Race—Criterion of prematurity: birth weight less than 5 pounds 3 ounces (2,350 Gm.)									
Slight bleeding	48 (13%)	317	365	2 (50%)	2	4	50 (14%)	319	369
Placenta previa	38 (28%)	98	136	20 (71%)	8	28	58 (35%)	106	164
Premature separation	15 (36%)	27	42	12 (55%)	10	22	27 (42%)	37	64
Bleeding due to trauma	2 (20%)	8	10	0	0	0	2 (20%)	8	10
Total bleeding	103 (19%)	450	553	34 (63%)	20	54	137 (23%)	470	607
No bleeding	347 (7%)	4,871	5,218	66 (45%)	81	147	413 (8%)	4,952	5,365
Total number of patients	450 (8%)	5,321	5,771	100 (50%)	101	201	550 (9%)	5,422	5,972

The Negro infants were reclassified to include as premature only those whose birth weights were less than 5 pounds and 3 ounces (2,350 Gm.), in order to make prematurity among the offspring of

white and of Negro women more comparable in respect to stage of development. Our reasons for establishing these dual standards have been described in a previous report.[4] With such a revised classification, the incidence of premature deliveries by Negro women with no history of uterine bleeding during pregnancy was 8 per cent, similar to the rate in the corresponding group of white women. Slight uterine bleeding was followed by premature delivery at approximately the same rate as occurred in the white women. Placenta previa was associated with a slightly higher incidence of prematurity among the offspring of Negro

TABLE 2.—*Comparison of Incidence of Premature Births to Women with Various Types of Uterine Bleeding and to Women with No Bleeding (Live-Born and Stillborn) (Single Births Only)*

	χ^2	P	Significance of Observed Differences
White Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)			
Bleeding vs. no bleeding	224.2	Very small	Highly significant
Slight bleeding vs. no bleeding	33.2	Very small	Highly significant
Slight bleeding vs. placenta previa	26.3	Very small	Highly significant
Slight bleeding vs. premature separation	76.7	Very small	Highly significant
Placenta previa vs. premature separation	15.3	0.00009	Very significant
Negro Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)			
Bleeding vs. no bleeding	120.9	Very small	Highly significant
Slight bleeding vs. no bleeding	19.5	Very small	Very significant
Slight bleeding vs. placenta previa	19.9	Very small	Very significant
Slight bleeding vs. premature separation	24.2	Very small	Highly significant
Placenta previa vs. premature separation	1.7	0.19	Not significant
Negro Race—Criterion of prematurity: birth weight less than 5 pounds 3 ounces (2,350 Gm.)			
Bleeding vs. no bleeding	142.5	Very small	Highly significant
Slight bleeding vs. no bleeding	15.2	0.0001	Very significant
Slight bleeding vs. placenta previa	32.1	Very small	Highly significant
Slight bleeding vs. premature separation	28.7	Very small	Highly significant
Placenta previa vs. premature separation	0.6	0.42	Not significant

mothers than among those of white mothers, and premature separation of the placenta with a slightly lower incidence. The differences occurring in the last two categories are not statistically significant (table 2).

Labor was induced prematurely by a physician in 26 patients who had symptoms of bleeding. Sixteen of the women were white, and 10 were Negro. In 2 of the white patients cesarean section was performed. Bleeding was the only abnormal symptom in 18 mothers of the group, and in the remainder toxemia and other abnormal conditions were also present. None of the patients was excluded from the series under con-

4. Brown, E. W.; Lyon, R. A., and Anderson, N. A.: Causes of Prematurity: V. The Influence of Syphilis on the Incidence of Prematurity, Am. J. Dis. Child. **70**:318 (Nov.-Dec.) 1945; VI. The Influence of Toxemia on the Incidence of Prematurity, ibid. **71**:378 (April) 1946.

sideration, because the condition producing bleeding seemed to be the underlying factor responsible for the premature delivery of the infants.

Mothers Whose Only Abnormality of Pregnancy Was Uterine Bleeding.—To obtain a more accurate estimate of the association between

TABLE 3.—*Incidence of Premature Births to Women Who Had Some Type of Abnormal Uterine Bleeding as the Only Abnormality of Pregnancy (Single Births Only)*

	Live-Born			Stillborn			Live-Born and Stillborn		
	Premature	Full Term	Total	Premature	Full Term	Total	Premature	Full Term	Total
White Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)									
Slight bleeding	56 (14%)	343	399	7 (70%)	3	10	63 (15%)	346	409
Placenta previa	35 (24%)	111	146	11 (73%)	4	15	46 (29%)	115	161
Premature separation	31 (50%)	31	62	7 (100%)	0	7	38 (55%)	31	69
Bleeding due to trauma	2 (14%)	12	14	2 (100%)	0	2	4 (25%)	12	16
Total bleeding	124 (20%)	497	621	27 (79%)	7	34	151 (23%)	504	655
Normal mothers	201 (5%)	3,805	4,006	21 (57%)	16	37	222 (5%)	3,821	4,043
Negro Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)									
Slight bleeding	36 (16%)	187	223	1 (50%)	1	2	37 (16%)	188	225
Placenta previa	21 (26%)	59	80	5 (56%)	4	9	26 (29%)	63	89
Premature separation	7 (37%)	12	19	7 (70%)	3	10	14 (48%)	15	29
Bleeding due to trauma	0	5	5	0	0	0	0	5	5
Total bleeding	64 (20%)	263	327	13 (62%)	8	21	77 (22%)	271	348
Normal mothers	244 (9%)	2,588	2,832	19 (54%)	16	35	263 (9%)	2,604	2,867
Negro Race—Criterion of prematurity: birth weight less than 5 pounds 3 ounces (2,350 Gm.)									
Slight bleeding	27 (12%)	196	223	1 (50%)	1	2	28 (12%)	197	225
Placenta previa	20 (25%)	60	80	4 (44%)	5	9	24 (27%)	65	89
Premature separation	7 (37%)	12	19	5 (50%)	5	10	12 (41%)	17	29
Bleeding due to trauma	0	5	5	0	0	0	0	5	5
Total bleeding	54 (17%)	273	327	10 (50%)	11	21	64 (18%)	284	348
Normal mothers	145 (5%)	2,687	2,832	18 (51%)	17	35	163 (6%)	2,704	2,867

uterine bleeding and premature delivery, a group of patients was selected who had no detectable illness or abnormality which might have caused premature labor other than bleeding. There were 655 white patients who belonged in this category and 4,043 other patients who had entirely normal pregnancies. The prematurity rate among the offspring of the group having normal pregnancies was 5 per cent. When mild bleeding

occurred as the only abnormality of pregnancy, the prematurity rate rose to 15 per cent; with placenta previa it was 29 per cent, and with premature separation of the placenta it was 55 per cent (table 3). All these differences were of definite significance (table 4). From these data it was evident that whenever bleeding occurred, either alone or in association with other maternal illnesses, the rates of prematurity were elevated to approximately the same levels.

Among the Negro women there were 348 who had uterine bleeding as the only abnormality of pregnancy and 2,867 patients who were

TABLE 4.—*Comparison of Incidence of Premature Births to Women with Bleeding as the Only Abnormality of Pregnancy and to Women Whose Histories Were Normal (Live-Born and Stillborn) (Single Births Only)*

	χ^2	P	Significance of Observed Differences
White Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)			
Bleeding vs. normal	235.5	Very small	Highly significant
Slight bleeding vs. normal	59.3	Very small	Highly significant
Slight bleeding vs. placenta previa	12.1	0.0005	Very significant
Slight bleeding vs. premature separation	53.4	Very small	Highly significant
Placenta previa vs. premature separation	13.5	0.0002	Very significant
Negro Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)			
Bleeding vs. normal	53.7	Very small	Highly significant
Slight bleeding vs. normal	11.8	0.0006	Very significant
Slight bleeding vs. placenta previa	5.7	0.02	Significant
Slight bleeding vs. premature separation	14.3	0.0002	Very significant
Placenta previa vs. premature separation	2.7	0.10	Not significant
Negro Race—Criterion of prematurity: birth weight less than 5 pounds 3 ounces (2,350 Gm.)			
Bleeding vs. normal	74.4	Very small	Highly significant
Slight bleeding vs. normal	15.3	0.00009	Highly significant
Slight bleeding vs. placenta previa	8.7	0.003	Very significant
Slight bleeding vs. premature separation	14.1	0.0002	Very significant
Placenta previa vs. premature separation	1.5	0.22	Not significant

entirely well during pregnancy. The incidence of prematurity was 9 per cent among the offspring of the latter group of women. It rose to 16 per cent when the mothers had symptoms of slight bleeding and to 29 per cent and 48 per cent respectively in the groups with placenta previa and premature separation of the placenta (table 3).

When the standard of prematurity for Negro infants was adjusted to include only those infants with birth weights of less than 5 pounds and 3 ounces (2350 Gm.), the incidence of premature deliveries by the patients with normal pregnancies was 6 per cent, almost identical with that of the white women. Associated with slight uterine bleeding was a prematurity rate of 12 per cent; with placenta previa, a rate of 27 per cent, and with premature separation of the placenta, a rate of 41 per cent.

The number of stillbirths in both racial groups was small. Among the white patients, uterine bleeding was associated with a slight increase of the incidence of premature stillbirth, but the number of patients was so small that the differences were not significant. In the Negro race the incidence of premature stillbirth was definitely increased among the offspring of mothers who suffered from uterine bleeding (tables 3 and 4).

TABLE 5.—*Incidence of Premature Births to Women Who Had Slight Bleeding as the Only Abnormality of Pregnancy (Single Births Only)*

	Live-Born			Stillborn			Live-Born and Stillborn		
	Premature	Full Term	Total	Premature	Full Term	Total	Premature	Full Term	Total
White Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)									
Spotting	30 (11%)	249	279	6 (86%)	1	7	36 (13%)	250	286
Continued menses	12 (23%)	40	52	0	1	1	12 (23%)	41	53
Early bleeding	14 (21%)	54	68	1 (50%)	1	2	15 (21%)	55	70
Total slight bleeding	56 (14%)	343	399	7 (70%)	3	10	63 (15%)	346	409
Normal mothers	201 (5%)	3,805	4,006	21 (57%)	16	37	222 (5%)	3,821	4,043
Negro Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)									
Spotting	27 (16%)	146	173	1 (50%)	1	2	28 (16%)	147	175
Continued menses	5 (21%)	19	24	0	0	0	5 (21%)	19	24
Early bleeding	4 (15%)	22	26	0	0	0	4 (15%)	22	26
Total slight bleeding	36 (16%)	187	223	1 (50%)	1	2	37 (16%)	188	225
Normal mothers	244 (9%)	2,588	2,832	19 (54%)	16	35	263 (9%)	2,604	2,867
Negro Race—Criterion of prematurity: birth weight less than 5 pounds 3 ounces (2,350 Gm.)									
Spotting	21 (12%)	152	173	1 (50%)	1	2	22 (13%)	153	175
Continued menses	4 (17%)	20	24	0	0	0	4 (17%)	20	24
Early bleeding	2 (8%)	24	26	0	0	0	2 (8%)	24	26
Total slight bleeding	27 (12%)	196	223	1 (50%)	1	2	28 (12%)	197	225
Normal mothers	145 (5%)	2,687	2,832	18 (51%)	17	35	163 (6%)	2,704	2,867

Since significantly higher rates of premature birth were associated with a history of even slight bleeding as the only abnormality of pregnancy, an attempt was made to subdivide this group and search for the cause. "Slight bleeding" as stated previously included such symptoms as very slight or occasional spotting or bleeding, continued menses and unexplained bleeding before the last trimester. Among both the white and the Negro patients even the mildest type of occasional spotting

TABLE 6.—*Incidence of Premature Births to Women Whose Pregnancies Were Complicated by Bleeding Alone or Associated with Some Other Abnormality (Single Births Only)*

	Live-Born			Stillborn			Live-Born and Stillborn		
	Premature	Full Term	Total	Premature	Full Term	Total	Premature	Full Term	Total
White Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)									
Bleeding only	124 (20%)	497	621	27 (79%)	7	34	151 (23%)	504	655
Bleeding and toxemia	25 (20%)	101	126	7 (64%)	4	11	32 (23%)	105	137
Bleeding and syphilis	11 (28%)	28	39	1 (100%)	0	1	12 (30%)	28	40
Bleeding, toxemia and syphilis	1 (13%)	7	8	0	0	0	1 (13%)	7	8
Bleeding, toxemia and other disorder	3 (15%)	17	20	0	1	1	3 (14%)	18	21
Bleeding, syphilis and other disorder	0	0	0	1 (100%)	0	1	1 (100%)	0	1
Bleeding, toxemia, syphilis and other disorder	0	4	4	1 (100%)	0	1	1 (20%)	4	5
Bleeding and other disorder	6 (10%)	57	63	1 (33%)	2	3	7 (11%)	59	66
Total bleeding	170 (19%)	711	881	38 (73%)	14	52	208 (22%)	725	933
Negro Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)									
Bleeding only	64 (20%)	263	327	13 (62%)	8	21	77 (22%)	271	348
Bleeding and toxemia	17 (23%)	56	73	8 (89%)	1	9	25 (30%)	57	82
Bleeding and syphilis	17 (23%)	56	73	8 (89%)	1	9	25 (30%)	57	82
Bleeding, toxemia and syphilis	6 (29%)	15	21	6 (86%)	1	7	12 (43%)	16	28
Bleeding, toxemia and other disorder	4 (44%)	5	9	1 (50%)	1	2	5 (45%)	6	11
Bleeding, syphilis and other disorder	7 (50%)	7	14	2 (100%)	0	2	9 (56%)	7	16
Bleeding, toxemia, syphilis and other disorder	2 (40%)	3	5	1 (50%)	1	2	3 (43%)	4	7
Bleeding and other disorder	10 (32%)	21	31	0	2	2	10 (30%)	23	33
Total bleeding	127 (23%)	426	553	39 (72%)	15	54	166 (27%)	441	607
Negro Race—Criterion of prematurity: birth weight less than 5 pounds 3 ounces (2,350 Gm.)									
Bleeding only	54 (17%)	273	327	10 (48%)	11	21	64 (18%)	284	348
Bleeding and toxemia	10 (14%)	63	73	8 (89%)	1	9	18 (22%)	64	82
Bleeding and syphilis	15 (21%)	58	73	7 (78%)	2	9	22 (27%)	60	82
Bleeding, toxemia and syphilis	5 (24%)	16	21	6 (86%)	1	7	11 (39%)	17	28
Bleeding, toxemia and other disorder	3 (33%)	6	9	1 (50%)	1	2	4 (36%)	7	11
Bleeding, syphilis and other disorder	7 (50%)	7	14	2 (100%)	0	2	9 (56%)	7	16
Bleeding, toxemia, syphilis and other disorder	2 (40%)	3	5	0	2	2	2 (29%)	5	7
Bleeding and other disorder	7 (23%)	24	31	0	2	2	7 (21%)	26	33
Total bleeding	103 (19%)	450	553	34 (63%)	20	54	137 (23%)	470	607

resulted in a significant increase in the number of premature births. Continued menses and early unexplained bleeding were associated with still higher rates for the white women but occurred in too few Negro patients to permit any definite conclusions. It is reasonable to suppose that if the numbers of Negro patients in the latter group were increased the premature birth rates would be similar to those for the white race (table 5).

Bleeding Associated with Other Disorders.—In 70 per cent of the white patients who had symptoms of bleeding during pregnancy the disorder was the only abnormality of pregnancy, and in the remaining

TABLE 7.—*Comparison of the Incidence of Premature Births to Women Who Had Bleeding Only and Bleeding Associated with Toxemia or Syphilis (Live-Born and Stillborn) (Single Births Only)*

	χ^2	P	Significance of Observed Differences
White Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)			
Bleeding only vs. bleeding and toxemia	0.0012	0.97	Not significant
Bleeding only vs. bleeding and syphilis	0.66	0.42	Not significant
Bleeding only vs. bleeding, toxemia and syphilis	Cases too few for statistical evaluation		
Negro Race—Criterion of prematurity: birth weight less than 5 pounds 8 ounces (2,500 Gm.)			
Bleeding only vs. bleeding and toxemia	2.12	0.15	Not significant
Bleeding only vs. bleeding and syphilis	2.12	0.15	Not significant
Bleeding only vs. bleeding, toxemia and syphilis	6.40	0.01	Significant
Negro Race—Criterion of prematurity: birth weight less than 5 pounds 3 ounces (2,350 Gm.)			
Bleeding only vs. bleeding and toxemia	0.34	0.56	Not significant
Bleeding only vs. bleeding and syphilis	2.45	0.12	Not significant
Bleeding only vs. bleeding, toxemia and syphilis	5.84	0.02	Significant

30 per cent bleeding occurred in association with various other disorders. It was not more frequently observed in the women with toxemia or syphilis than in those who suffered from other diseases. The incidence of bleeding in the women with toxemia, in those with syphilis and in those who had neither syphilis nor toxemia but some other abnormality was about 13 per cent for each group (table 6). Likewise, the incidence of premature delivery was not significantly different in groups of women who suffered from toxemia or syphilis in addition to bleeding than in the group of women whose bleeding was the only abnormality of pregnancy (table 7).

Among the Negro women only 57 per cent of the patients with a history of some form of bleeding had the symptom as the only abnormality of pregnancy. The prematurity rate among the offspring of this group was 22 per cent. It rose slightly, to 30 per cent, when either syphilis or toxemia occurred as an added illness of pregnancy. When bleed-

ing, syphilis and toxemia all occurred in the same patient, the prematurity rate was increased to 43 per cent (tables 6 and 7).

These data are in contrast to those noted in our studies of prematurity among the offspring of women suffering from syphilis and toxemia (part V). In these groups other abnormalities in addition to the one under consideration invariably resulted in an increased rate of prematurity. In view of the evident importance of bleeding as a predisposing factor of prematurity, it would be desirable to examine in more detail the type of bleeding which is associated with various grades of toxemia, with treated and untreated syphilis and with various other acute and chronic conditions. Such information will be available only when subdivided groups are large enough to permit statistical treatment.

SUMMARY AND CONCLUSIONS

1. The occurrence of uterine bleeding during pregnancy was accompanied with a decided increase of the incidence of prematurity. Among the offspring of white women who had only the mildest form of bleeding the rate of prematurity was 14 per cent; among the offspring of those with placenta previa the rate was 30 per cent, and among the offspring of those with premature separation of the placenta the rate was 53 per cent. These rates were in distinct contrast to that of 7 per cent, the rate of premature deliveries by the group of women who had no symptoms of bleeding throughout pregnancy. In the Negro women uterine bleeding during pregnancy occurred less often than in the white women, but the incidence of prematurity was approximately the same among the offspring of the two groups. This was especially true when prematurity among Negro infants was restricted to those whose birth weight was less than 5 pounds and 3 ounces (2,350 Gm.).

2. For a more accurate test of the association between uterine bleeding and the incidence of prematurity, the women whose only abnormality of pregnancy was bleeding were placed in a separate group. Among the white women of this series who had mild bleeding the incidence of prematurity was 15 per cent; among those with placenta previa it was 29 per cent, and among those with premature separation of the placenta it was 55 per cent. The incidence of prematurity among the offspring of women who had no abnormalities during pregnancy was 5 per cent. In the Negro race the rates were approximately the same.

3. The occurrence of other illnesses, such as toxemia of pregnancy or syphilis, together with bleeding did not increase the incidence of prematurity above the levels associated with bleeding alone.

4. The conditions responsible for uterine bleeding during pregnancy have a more decided influence on the incidence of prematurity than any of the other illnesses commonly associated with pregnancy.

NEW TYPE OF FAMILIAL CONGENITAL CHRONIC HEMOLYTIC ANEMIA

EUGENE STRANSKY, M.D.
AND
ARSENIO C. REGALA, M.D.
MANILA, PHILIPPINE ISLANDS

IN the year 1940 we submitted a paper on chronic familial hemolytic anemia to the *Acta Medica Philippina* for publication. Unfortunately, no new issues could appear after the war started in the Far East. In 1945, when the Americans liberated the Philippine Islands, the office of the *Acta* was burned and the editor killed. In the year 1942, we published a paper [1] on erythroblastic anemia following splenectomy in cases of chronic familial hemolytic anemia. We described 2 observed cases in which erythroblastosis developed after splenectomy. In the following years we studied this response to splenectomy thoroughly and were able to establish facts which prove that we are dealing with a definite clinical entity not described until now. There are cases of so-called atypical hemolytic anemias in the literature. Our cases, however, do not at all correspond to these cases. We are aware that our observations are still incomplete, and we have had to do our work under strain and with a lack of laboratory facilities. During the Japanese occupation no reagents and no x-ray plates were at our disposal, with the exception of the rapidly dwindling old stocks. Furthermore, in February 1945, the archives of the Philippine General Hospital were burnt and the protocols of the clinical conferences were likewise destroyed. We can therefore refer to our files only so far as they were not destroyed or looted.

We decided to publish our observations after we had had a chance to get the interesting paper of Dr. Thomas B. Cooley [2] on a new type of hereditary anemia with elliptocytosis. In 1 case splenectomy was done; after the removal of the spleen there was no improvement of the hemolysis and hemolytic crises developed again. Our cases have in common with those of Cooley that splenectomy did not help at all; in other respects they are, however, quite different. We shall discuss

From the Department of Pediatrics, College of Medicine, University of the Philippines.

1. Stransky, E., and Regala, A. C.: Erythroblastic Anemia Following Splenectomy in Cases of Chronic Familial Hemolytic Anemia, Am. J. Dis. Child. **63**:859 (May) 1942.

2. Cooley, T. B.: A Severe Type of Hereditary Anemia with Elliptocytosis: Interesting Sequence of Splenectomy, Am. J. M. Sc. **209**:561, 1945.

the differences after we have described the symptoms in the observed cases and after we have furnished arguments in favor of the supposition that in our cases we are dealing with a definitely new type of hemolytic anemia, chronic, familial and inherited.

In April 1940 we had a chance to observe 4 cases of hemolytic anemia among five children in the same family. One of these cases was described in our former paper, in 1942. The first child of the family, a boy of 11 years, was healthy; all the others showed distinct symptoms of a more or less severe anemia. The mother was suffering from an iron deficiency anemia, which had, however, nothing in common with the anemia of the siblings. The father did not show anemia; his red blood cell count, hemoglobin level and differential count were normal at the time of examination; there had been, however, noticeable anisocytosis, the icterus index was 11.9 units and the van den Bergh reaction was positive, although indirect and delayed; the reticulocytes were as high as 6 per cent. The youngest of the 5 children, a baby at this time only 5 months of age, on examination showed a red cell count of 3,200,000 per cubic millimeter with 10 Gm. of hemoglobin per hundred cubic centimeters. There were, however, 21 nucleated red cells counted among 250 white cells, while in the bone marrow there were 752 nucleated red cells to 250 white cells. There were plenty of proerythroblasts and other immature forms of nucleated red cells. Another child, a boy, 6 years of age, showed around 100 nucleated red cells to 250 white cells in the peripheral blood, while another boy, 9 years of age, still had 24 nucleated red cells to 250 white cells. The most serious case was that of a girl, at this time 8 years of age, with a hemoglobin content of 4.5 Gm. per hundred cubic centimeters and 1,500,000 red cells per cubic millimeter with 75 nucleated red cells to 250 white cells in the peripheral blood. The white cell count (with the nucleated red cells) was 15,700 per cubic millimeter. There were proerythroblasts and mitotic red cells in the peripheral blood. The constituents of the bone marrow in all 4 children were practically identical. The boy of 9 years of age showed 325 nucleated red cells to 250 white cells; the girl of 8 years, 592 to 250 and the boy of 6 years, 366 red cells to 250 white cells. In all cases, there were plenty of mitotic cells and proerythroblasts in the bone marrow. Fragility of the red cells was normal in all cases: incomplete hemolysis in a solution of 0.26 to 0.28 per cent sodium chloride and complete hemolysis at a concentration of 0.40 to 0.42 per cent. There were in all cases pronounced anisocytosis and polychromasia in the blood smear but no evidence of spherocytosis. The volume of the red cells was normal, around 80 to 90 cubic microns. The icterus index was invariably high, around 15 units, and the van den Bergh reaction was delayed and indirect. It may be emphasized that the percentage of reticulocytes

was high in all 4 cases, ranging between 10 to 20 per cent. While the baby was not yet jaundiced, the 3 other children were definitely icteric. Results of urinary examination were characteristic for hemolytic anemia, with increased discharge of urobilinogen and no bile pigments. The feces were of normal color. Quantitative studies of pigment were not done. There was a history of hemolytic crises in the children 6, 8 and 11 years of age. All 4 children had a noticeable enlargement of the spleen. The observations given so far are all in favor of chronic familial hemolytic anemia. The erythroblastosis is, however, striking. In chronic familial hemolytic anemia, a few nucleated red cells may be observed in the peripheral blood. They are, however, never so numerous as in our observed cases. Furthermore, Chauffard [3] has already coined the slogan that patients suffering from chronic, familial hemolytic anemia are more jaundiced than sick (*plus ictérique que malade*). Our patients were, however, very sick. The girl of 8 years had a red blood cell count of only 1,500,000, which is quite extraordinary in chronic, familial anemia. She was bedridden and extremely weak; her liver and heart were much enlarged and her legs slightly edematous. Although we were at a loss how to explain the causes of severe anemia and the erythroblastosis, we still believed we had to deal with a severe case of familial hemolytic anemia that might be atypical. At any rate, we suggested splenectomy, which was done Nov. 7, 1940. We have already reported on the result. After splenectomy, the anemia did not improve, the hemolytic crises persisted and the jaundice was not at all influenced. We have already published the results of examinations of the blood to August 1941; we have now to add and to compare the results during 1942 and 1944, two and four years after splenectomy.[4] The differential count (percentages) per cubic millimeter was as follows:

Date	B.	E.	M.	J.	St.	S.	L.	Mo.	Nucleated Red Cells		White Cells
3/13/40	...	2.4	8.0	6.0	8.4	27.2	30.0	1.2	75	:	250
10/11/40	...	1.2	1.6	3.6	12.4	46.4	31.6	3.2	35	:	250
11/ 7/40	Splenectomy										
11/16/40	2.8	12.0	0.4	0.8	6.0	34.4	36.4	7.2	34	:	250
11/28/40	1.2	8.4	2.4	2.4	9.6	40.0	26.4	9.2	2,402	:	250
12/17/40	...	11.2	0.8	2.0	14.8	30.4	40.0	6.4	6,900	:	250
3/ 4/41	2.4	15.2	...	0.8	6.0	42.4	32.4	3.2	2,207	:	250
3/21/41	1.2	4.0	...	2.4	4.0	43.6	46.0	1.2	1,056	:	250
4/ 3/41	2.0	2.4	2.8	2.0	9.6	32.0	38.8	7.2	1,434	:	250
11/ 8/41	1.6	14.8	0.4	0.4	1.2	35.2	34.4	5.6	1,726	:	250
7/19/42	0.8	4.4	0.8	0.8	8.0	54.4	24.8	4.8	4,427	:	250
11/ 2/44	1.2	3.6	0.4	5.2	6.0	56.0	30.0	2.0	6,079	:	250

The constant erythroblastosis can be well appreciated from this tabulation.

3. Chauffard, A.: Pathogénie de l'ictère congénital de l'adulte, Semaine méd. **27**:25, 1907.

4. The abbreviations used in these tabulations and in similar ones later in the paper have the following significance: B, basophils; E, eosinophils; M, myelocytes; J, juvenile cells; St., staff cells; S, segmented cells; L, lymphocytes; Mo, monocytes; N. R. C., nucleated red cells and W.C., white cells.

The child was readmitted for the third time, in July 1942. Because of the last hemolytic crisis, the red cell count was only 1,200,000 per cubic millimeter with 4.5 Gm. of hemoglobin per hundred cubic centimeters and 178,000 nucleated red cells per cubic millimeter. After the crisis, the red cell count rose to 2,075,000 and the hemoglobin to 7.3 Gm., but the erythroblastosis did not change and the ratio was still 4,750 nucleated red cells to 250 white cells. Two weeks later a red cell count of 2,524,000 and a hemoglobin level of 9 Gm. were reached; there were, however, 234,000 nucleated red cells per cubic millimeter and the white cell count was 12,000. After a second hemolytic crisis the red cell count dropped again to 1,800,000 and the number of nucleated red cells from 234,000 to 48,000 per cubic millimeter. Two weeks later, we again counted 2,300,000 erythrocytes and 153,000 erythroblasts per cubic millimeter. There was a constant macrocytosis. Before splenectomy, the mean corpuscular volume was 80 to 85 cubic microns; after the operation it rose to 130 to 135 cubic microns with a simultaneous hyperchromia, the color index being 13 to 1.4. The child left the hospital in September 1942, after an observation of two months, again unimproved. We saw her the last time in November 1944. At this time the food situation in Manila was already critical and the child was seriously undernourished and suffering from slight hunger edema. Examination of the blood now revealed a red cell count of 1,070,000, a nucleated cell count (including white cells and nucleated red cells) of 178,000 per cubic millimeter and a hemoglobin content of 3.4 Gm. per hundred cubic centimeters. As there were 6,079 nucleated red cells to 250 white cells, the real white cell count was not higher than around 8,000 cells. The differential count has already been reported. In the bone marrow, there were 6,095 nucleated red cells to 250 white cells and almost all the nucleated red cells were normoblasts. Further examinations gave the following results:

Volume of the packed red cells, per cent	15
Mean corpuscular volume, cubic microns	136
Mean corpuscular hemoglobin content, micromicrograms	32.4
Mean corpuscular hemoglobin concentration, per cent	25
Volume index	1.64
Color index	1.20
Saturation index	0.72

The serum protein level of her blood was 5.7 per cent with 2.7 per cent serum albumin and 3 per cent serum globulin. In a series of more than 30 cases of hypoproteinemia (unpublished studies of Eugene Stransky and Chenting Chin), on account of the starvation of the present time, microcytic, hypochromic anemia has been found as a constant characteristic. In our particular case there was, however, in spite of hypoproteinemia, still pronounced macrocytosis; the color index was already decreased, formerly having been always 1.3 to 1.4, while there was definitely a decrease of the hemoglobin measured on

the saturation index, which was 0.72. It may be stressed, therefore, that the macrocytosis did not change at all. Macrocytosis after splenectomy seems to be a constant characteristic of this kind of hemolytic anemia.

Ambrosio, first seen in 1940, a brother of our former patient, Sofia, had been admitted a second time on Jan. 3, 1943 at the age of 12 years. The chief complaints were a general body weakness, pallor, jaundice and recurrent abdominal pain. In the hospital a serious hemolytic crisis developed in the boy, so severe that the red cell count dropped to 920,000 cells per cubic millimeter, with 25 erythroblasts to 250 white cells and a hemoglobin level of 3 Gm. per hundred cubic centimeters. There was a noticeable erythropoietic hyperactivity of the bone marrow. After the crisis the red cell count increased to 1,500,000. Splenectomy was done on Feb. 16, 1943. We did not expect a recovery but rather an improvement of the general conditions and some benefit for the patient by a lessening of the hemolysis and the hemolytic crises. Just before splenectomy, there were 8 erythroblasts to 250 white cells. In two weeks after splenectomy the red cell count rose to 2,500,000 and in four weeks to 3,000,000 per cubic millimeter. There was, however, erythroblastosis with 1,195—at times, 3,600—erythroblasts to 250 white cells. There was likewise an immediate increase of the mean corpuscular volume from 82 before to 123 cubic microns four weeks after splenectomy! We took occasion, of course, to examine the spleen histologically.

Dr. Santa Cruz, the pathologist of the Cancer Institute, reported the following observations: "The surface of the spleen is irregular, owing to multiple pittings, and shallow as to color. The capsule is rather thick and the cut surface flat with a consistent pulp, brownish, with a very small amount of blood in the sinuses. On microscopic examination, a section of the spleen shows a thickened capsule and clear malpighian corpuscles, although most of the latter are atrophic. The splenic pulp is very cellular. The cords are widened and the sinuses conspicuous. There is an increased number of reticulum cells in the areas. In others the reticulum cells are hyperplastic and the endothelial cells also prominent to bring out the sinuses in the red pulp. There is much necrosis around the large blood vessels and the trabeculae. There are few red blood corpuscles in the sinuses and a scanty amount in the pulp. The prominent observations in this case are an increased hyperplasia of the reticular cells and reticular fibrils, that are the causes of the splenomegaly. There is no evidence of hematopoietic activity. The whole picture is completely different from the section of a spleen from a person with hemolytic anemia. The diagnosis is hyperplastic splenomegaly, compatible with Cooley's anemia."

To compare these results with the typical results in a case of hemolytic anemia, we would like to comment on the observations in the case of a 23 year old American sailor on whom a splenectomy was performed in March 1942. There was, of course, a complete recovery after the splenectomy. The following observations were made by Dr. Santa Cruz: "The spleen weighs 2,085 Gm., measuring 29 by 21 by 6 cm. It is soft and rather flabby, and the capsule is thick, grayish brown and smooth, except the upper fold where areas of gray thickening were noticed. The cut surface exudes plenty of thin fluid and bulges on sectioning. The splenic pulp is brownish and mottled, with grayish trabeculae, which are slightly increased. A microscopic section of the spleen shows empty sinuses, which can be hardly distinguished. Splenic pulp packed with red blood cells has produced collapse of the sinuses. Lymphoid centers have disappeared. Reticuloendothelial cells are prominent. Fibrous trabeculae are increased and edematous, with calcification. Splenic arteries are thickened and edematous, with definite calcification in most of them."

In typical hemolytic anemia, there is an active hyperemia and the pulp is engorged with red cells, while in our case there was passive hyperemia, with blood in the sinuses.

In 1939, a splenectomy was performed on a Filipino boy of 11 years. We had a chance to see him again in 1943, although only for a few hours. We were able, however, to check the hematologic values again. In October 1939 the blood contained: 640,000 red cells per cubic millimeter; 5.6 Gm. of hemoglobin per hundred cubic centimeters and 29 to 36 per cent reticulocytes. The icterus index was 11.4 units. In the peripheral blood there were 14 to 24 erythroblasts to 250 white cells and definite anisocytosis and polychromasia. In the bone marrow there were 132.8 erythroblasts to 100 white cells. The fragility of the red cells was normal.

A splenectomy was performed on the patient Dec. 1, 1939. Examinations of the blood before and after the splenectomy gave the following results:

	11/11/39	11/28/39	12/12/39
Iron, milligrams	16	27	35
Hemoglobin, grams	4.7	8	10
Red cell count	1,605,000	3,420,000	3,980,000
Reticulocytes, per cent	22	17	5.6
Volume of the cells	12	24	28
Platelet count	225,000	270,000	980,000
Leukocyte count	8,400	6,000	12,300
Mean corpuscular volume, cubic microns	74	70	71
Mean corpuscular hemoglobin content, micromicrograms	29	23	71
Mean corpuscular hemoglobin concentration, per cent	39	33	35
Volume index	0.88	0.83	0.83
Color index	1.07	1.03	1.09
Saturation index	1.21	1.03	1.02
Icterus index, units	0	12	8.83

In the beginning, there were a very low cell count and hemoglobin level due to the hemolytic crisis; then there was a decided improvement after the exaggerated destruction of the red cells had been stopped. During the hemolytic crisis, there was a very high reticulocyte count, decreased, however, after the crisis. After splenectomy, a slight increase of the red cell count and hemoglobin level was noted. The noticeable rise of the thrombocyte count is a constant observation even in normal persons after splenectomy, owing to the removal of the thromboclastic activity of the spleen. In classic hemolytic anemias there is a tendency —absent, however, in our particular case—to increased corpuscular volumes of the erythrocytes on account of spherocytosis.

We considered the case as one of typical hemolytic anemia at this time. We saw the boy the next year; he was much improved, not jaundiced and not complaining any more of hemolytic crises and abdominal pains. In July 1943 the boy, then 13½ years old, came again, complaining of repeated attacks of fever, dizziness, jaundice and abdominal pain. The red blood cell count was not so low, still being 2,800,000 per cubic millimeter. The white cell count, however, was 58,000 on account of a pronounced erythroblastosis. There were more than 600 nucleated red cells to each 100 white cells counted, so many that the real white cell count was only 8,000, and there were 50,000 erythroblasts per cubic millimeter. There was simultaneously a striking macrocytosis. Unfortunately, the boy left the hospital against advice, and we were unable to complete our examinations. At any rate, we have here again an instance of erythroblastosis, with constant jaundice and hemolytic crises four years after splenectomy.

The youngest child, admitted on account of a severe, chronic hemolytic anemia, was a Filipino boy 2 years and 3 months of age. He was admitted Nov. 20, 1942, with the chief complaints of enlargement of the abdomen and pallor. Three months previous to admission, attacks of fever developed in the child, lasting one to two weeks. He gradually became pale and much jaundiced.

The most important observations at admission were: a bulging abdomen, the spleen palpable, 1 fingerbreadth above the iliac crest, and liver palpable, 1 fingerbreadth below the right costal arch. The red blood cell count was 1,090,000 and the white cell count, 11,200 per cubic millimeter. The differential count was as follows:

B.	E.	M.	J.	St.	S.	L.	Mo.	Pl.[5]
..	0.4	..	..	3.6	50.0	30.6	4.4	2.0

5. Abbreviations not given in footnote 4, used in this and the following tabulations, are the following: Pl, platelets; Mbl, megaloblasts; Prom, promyelocytes; End, endothelial cells and Mit, mitotic cells.

There was a ratio of 8 nucleated red cells to 250 white cells. Extreme anisocytosis, and marked polychromasia were present, with a tendency to microcytosis. The cell count for the bone marrow was 96,800 per cubic millimeter of aspirated marrow. A smear of bone marrow revealed the following contents:

B.	E.	Mbl.	Prom.	M.	J.	St.	S.	L.	Mo.	End.
0.8	12.8	4.4	6.4	14.8	17.6	15.6	19	6.8	..	0.8

The ratio of nucleated red cells in the bone marrow to white cells was 459 to 250, among them 12 mitotic cells. On account of the severe anemia, we did not consider in this case the possibility of the classic type of chronic familial hemolytic anemia. There were 4 older children in the family; they were all healthy without any sign of blood dyscrasia. We decided to give the child the chance of splenectomy, although we knew that he might die after the intervention. On the other hand, we were convinced that without surgical intervention there was no hope for survival. Hence, after blood transfusion, splenectomy was performed.

The child died thirty-six hours after splenectomy. The postmortem observations were completely noncontributory; therefore there is no doubt that the patient died of anemia and possibly of postoperative shock. We took the opportunity to examine the spleen. The spleen (examined by Dr. Santa Cruz) showed passive hyperemia, the pulp engorged with blood, the sinuses empty and the fibrosis pronounced. Hence, there was no doubt that we had to deal with the same disease observed by us in the cases formerly described.

In our paper in 1942 we published another case of erythroblastosis after splenectomy; the case is a further instance of the same type of chronic familial hemolytic anemia. There has been a second child in this family (there were in all 2 children) with manifest symptoms of chronic hemolytic anemia, clinically and hematologically, at the age of 2 years. This patient was, however, not admitted and therefore not closely observed.

In June 1944, we were called to the medical ward to give our opinion of the condition of a Filipino woman, 27 years of age, suffering from severe anemia, and to suggest a suitable therapy. The history and the clinical observations suggested chronic familial, hemolytic anemia. We decided to restrict ourselves to our observations. They were as follows: red blood cell count 1,230,000 per cubic millimeter; hemoglobin level, 3 Gm. per hundred cubic centimeters; a differential count as follows:

B.	E.	M.	J.	St.	S.	L.	Mo.
..	..	..	0.4	4.8	31.2	28.8	4.8

a ratio of 8 nucleated red cells to 250 white cells; extreme anisocytosis, polychromasia and poikilocytosis, and fragmentation of the red cells. Further examinations revealed:

Volume of the packed red cells, per cent	10
Mean corpuscular volume, cubic microns	81.3
Mean corpuscular hemoglobin content, micromicrograms	24.4
Mean corpuscular hemoglobin concentration, per cent	30
Volume index	0.95
Color index	0.875
Saturation index	0.88
Reticulocytes, per cent	2 !

The differential count (percentages) per cubic millimeter of bone marrow was as follows:

B.	E.	Mbl.	Prom.	M.	J.	St.	S.	L.	Mo.	End.	Mit.
..	7.6	3.6	9.6	14.0	16.8	18.4	21.2	5.2	0.4	2.4	0.8

Normoblasts	191
Basophilic erythroblasts	189 (!)
Macroblasts	157 (!)
Proerythroblasts	189 (!)
Megaloblasts	1
Mitotic red cells	43 (!)

The ratio of nucleated red cells to white cells was 780 : 250, or 312 nucleated red cells to 100 white cells. There were basophilic stipplings in the normoblasts, Many Howell-Jolly bodies were present. The megakaryocytes were normal. The bone marrow findings were remarkable. There was an extreme erythroblastosis. In normal bone marrow smears, around 80 per cent of the erythroblasts are normoblasts; in this particular case there was less than 25 per cent of normoblasts! There was a striking amount of mitotic red cells. There was also a preponderance of immature erythroblasts. Furthermore, the low percentage of reticulocytes was very important. Together with the low percentage of normoblasts, it was an evidence that the maturation of the red cells was impaired. While in typical cases of chronic familial hemolytic anemia the erythroblastic activity of the bone marrow is exaggerated, the maturation of the red cells is normal. The majority of the erythroblasts in the bone marrow are normoblasts, as in normal bone marrow, and the reticulocyte count in the peripheral blood is invariably high. Therefore we did not suggest splenectomy in this particular case. Unfortunately, in the chaotic circumstances prior to the collapse of the Japanese and the destruction of Manila, we were unable to follow up this interesting case. We have been able to establish the diagnosis, however, by means of the characteristic blood and bone marrow changes, entirely different from the classic type of hemolytic anemia.

In our material so far, we have had 3 cases of classic familial hemolytic anemia, with characteristic clinical and hematologic observations (with histologic examination of the removed spleen) among white

people and only 1 characteristic case with typical response to splenectomy among Filipinos. On the other hand, there were 10 typical cases of the new type of hemolytic anemia among Filipinos and no case among white people. We have 4 more cases of Filipinos on whom splenectomies have been performed; in these cases we are unable to state whether we have to deal with the classic type or with the new type of hemolytic anemia, as follow-up was not possible and the protocols with the histologic sections of the spleens were destroyed by fire.

The hemolytic anemia observed among native Filipinos seems to be an inherited, congenital disease, affecting (unlike the elliptocytotic anemia of Cooley) both sexes. Anemia, jaundice and splenomegaly seem to develop in early infancy. The peripheral blood is characterized by severe anemia, oligocythemia, oligochromemia, extreme anisocytosis and polychromasia. There is neither spherocytosis nor formation of target cells. Erythroblastosis is a conspicuous symptom. In the peripheral blood, erythroblastosis is constantly observed, although the number of erythroblasts seems to be rather moderate. The differential count shows a shift to the left of the neutrophils; myelocytes, sometimes myeloblasts and promyelocytes are present in the majority of cases. The icterus index of the blood serum is slightly increased (between 10 and 20 units), the bilirubin, quantitatively determined, is around 1.5 to 2 mg. per hundred cubic centimeters. Jaundice is present constantly, although the icterus is more prominent, naturally, during the frequent hemolytic crises. It must not be stressed that the jaundice shows all characteristics of a hemolytic icterus. The differential diagnosis, if we have to deal with the classic type of hemolytic anemia or with the type observed frequently among Filipinos, can be made to a certain degree by the examination of the peripheral blood. Severe anemia, early start of the disease, constant jaundice and, invariably, normal fragility of the cells without any changes in the amplitude between initial and complete hemolysis are in favor of the latter type. We can get more information and certainty by examination of the bone marrow. Erythropoietic hyperactivity is a consequence of increased hemoclasia in any kind of hemolytic anemia. The maturation of the red cells is, however, normal in typical cases of hemolytic anemia. There is a decided increase of the erythropoietic tissue; the distribution of the different stages of maturation of the erythroblasts is, however, not impaired. In our patients there was an increase of the immature elements of the erythroblasts in the bone marrow, so much so, that we got the impression that there was something wrong with the maturation of the red cells. Therefore, it may happen that the reticulocyte count is only slightly increased, although there is an extreme erythroblastosis in the bone marrow and a still marked erythroblastosis in the peripheral

blood. The differences in the histologic structure of the spleen in the two types have been already commented on. As the changes in the spleen were probably secondary in our cases, they are not considered characteristic of the disease; they are found in erythroblastic (Mediterranean) anemia and in the so-called Banti's syndrome. Very characteristic of our type of hemolytic anemia is the further development of the disease after splenectomy. In 3 cases, so far, after splenectomy there has been no improvement at all; hemolytic crises have continued to develop from time to time after an initial improvement of anemia and jaundice, and there has been no benefit to the patient from removal of the spleen. Moreover, an erythroblastosis has developed immediately after splenectomy lasting for years. Erythroblasts, numbering 50,000 to 200,000, have been constantly counted in the peripheral blood, although the reticulocyte count has not corresponded with this high count of nucleated red cells. Anisocytosis and polychromasia have grown worse after splenectomy. While prior to splenectomy the mean corpuscular volume of the red cells had been constantly around normal or even below normal, after splenectomy one could observe in the blood smear a striking macrocytosis, and the determination of the volume of the cells showed a mean corpuscular volume of around 135 cubic microns, higher even than observed in cases of sprue or pernicious anemia. As there was an extreme anisocytosis and plenty of microcytes were present, one can imagine how large the erythrocytes were. In spite of the macrocytosis, there were no megaloblasts in the bone marrow; on the contrary, there was a pronounced erythroblastosis of the bone marrow, but in contrast to the observations before removal of the spleen almost all the cells were mature normoblasts, although much bigger than normoblasts in healthy persons. We are sorry not to be able to illustrate our observations by photomicrographs; unfortunately, all the slides were lost, and during the Japanese occupation we had no films for pictures. The described hematologic changes after splenectomy are without any doubt due directly or indirectly to the removal of the spleen. Further observations may explain better these changes. At any rate, we learned that the spleen may have an influence on the size and maturation of the red cells in the bone marrow.

Not wishing to be misunderstood, we should like to emphasize that this action of the spleen is not observed in normal persons. We had an opportunity to study for years cases in which splenectomy was performed, on account of traumatic rupture of the spleen. After splenectomy there was sometimes a slight temporary erythroblastosis; the erythropoietic activity of the bone marrow was decreased for months; there were no other changes. Therefore, the changes in our cases of

hemolytic anemia are not to be attributed to the removal of the spleen only. There must be primarily something wrong with the maturation of the red cells in the bone marrow; on account of this trouble, increased hemolysis leading to severe anemia takes place. If there is such trouble, the removal of the spleen may lead to consequences previously described.

As for differential diagnosis, we have yet to comment on the differences between the erythroblastic anemia, described by Cooley [6] in 1925, and our type of hemolytic anemia. Although there are reports from different countries on erythroblastic anemia, and the earlier conception that the disease affects only persons of Mediterranean extraction is not maintained any more, we did not see a single case of erythroblastic anemia in the Philippines and know the disease only from the literature and the blood smears sent to us from abroad. Erythroblastic anemia develops in early childhood and is characterized by the presence of a pronounced erythroblastosis in the peripheral blood. The nucleated red cells are, even in the peripheral blood, mostly immature erythroblasts, which are likewise preponderant in the bone marrow. There is, furthermore, an extreme anisocytosis and polychromasia in the peripheral blood. There is a peculiar hyperplasia of the bone marrow so severe that the bones of the skull are thickened, owing to the hyperplasia of the diploe. In the roentgenogram, the bone shadow has a comblike appearance, containing numerous spicula, which represent substantia spongiosa filled with marrow, while the substantia compacta is extremely thin. The long bones show similiar changes. Because of the anatomic changes in the bones, there is a peculiar configuration of the skull and face, characteristic of the disease, as described in the excellent nonograph of Lehndorff.[7] The disease has a duration of several years. Although there are plenty of cases of target cell anemia (Dameshek [8]) in adults, the severe attacks in children are almost all fatal. After splenectomy there is a slight improvement of the hemolytic process, but simultaneously a severe erythroblastosis develops, lasting until death. In our cases, likewise, extreme erythroblastosis was observed, having lasted so far for four years, without any improvement of the anemia; the histologic picture of the spleen

6. Cooley, T. B., and Lee, P.: A Series of Cases of Anemia in Children with Splenomegaly and Peculiar Changes in the Bones, Tr. Am. Pediat. Soc. **37**:29, 1925; cited by Cooley, T. B.; Witwer, E. R., and Lee, P.: Anemia in Children with Splenomegaly and Peculiar Changes in the Bones, Am. J. Dis. Child. **34**:347 (Sept.) 1927.

7. Lehndorff, H.: Die Erythroblastenanämie, Ergebn. d. inn. Med. u. Kinderh. **50**:568, 1936.

8. Dameshek, W.: "Target Cell" Anemia: Anerythroblastic Type of Cooley's Erythroblastic Anemia, Am. J. M. Sc. **200**:445, 1940.

is practically identical in both diseases. There are, however, striking differences between our cases and cases of erythroblastic anemia. Our patients show after splenectomy normoblastosis, even in the bone marrow, while in erythroblastic anemia the proerythroblastosis does not change after splenectomy; on the contrary, it grows worse. In our patients we looked for the characteristic bone changes; there was some rarefaction of the bones, but this was not different from the changes of the bone observed in typical cases of chronic, familial, hemolytic anemia. The most striking observation in our cases, the macrocytosis after splenectomy, has, so far, never been reported in erythroblastic anemia.

Drepanocytic, or sickle cell, anemia is another distinct type of hemolytic anemia. As in our cases no sickle cell formation was observed, there was no difficulty in distinguishing between the two types.

There are plenty of cases reported in the literature of patients with hemolytic anemias who show no improvement after splenectomy. There is no doubt that in the near future definite types of disease will be distinguished among those which are now called typical hemolytic anemias (Thompson,[9] Haden[10]). No cases have so far been reported with erythroblastosis and macrocytic response to splenectomy. These responses represent according to our opinion a definite entity of hemolytic anemia.

Acute hemolytic anemia (Lederer[11]) has nothing to do with our type of hemolytic anemia. This type of hemolytic anemia is not congenital and not familial. Stransky and Quintos in the Philippines observed 4 cases of acute hemolytic anemia in children and reported the cases in a seminar of the College of Medicine of the University of the Philippines in June 1944. It is not necessary to discuss the differential diagnosis; the differences are self explanatory.

SUMMARY

A definite, not hitherto described type of chronic familial hemolytic anemia is presented. This kind of hemolytic anemia is characterized by the early appearance and by the severity of the symptoms. There is a constant erythroblastosis in the peripheral blood. The bone marrow shows an extreme erythroblastosis with a preponderance of immature

9. Thompson, W. P.: Hemolytic Jaundice, Bull. New York Acad. Med. **15**:177, 1939.

10. Haden, R. L.: Hemolytic Anemia, J. Lab. & Clin. Med. **26**:65, 1939.

11. Lederer, M.: Form of Acute Hemolytic Anemia, Probably of Infectious Origin, Am. J. M. Sc. **170**:500, 1925; Three Additional Cases of Acute Hemolytic (Infectious) Anemia, ibid. **179**:228, 1930.

erythroblasts. There is no spherocytosis and the fragility of the red cells is invariably normal. The type of anemia is microcytic and hypochromic. After splenectomy, there is no improvement of the anemia and jaundice; the anemia, however, changes its character, becoming macrocytic and hyperchromic. After removal of the spleen, an extreme erythroblastosis develops with up to 200,000 erythroblasts per cubic millimeter of blood. So far the disease has been observed only among Filipinos. The hematologic observations, clinical symptoms and differential diagnosis of this anemia are discussed.

TREATMENT OF INFANTILE CONGENITAL SYPHILIS WITH PENICILLIN

ALBERT HEYMAN, M.D.
AND
JOSEPH YAMPOLSKY, M.D.
ATLANTA, GA.

ALTHOUGH preliminary reports indicate that penicillin is of value in the treatment of early congenital syphilis,[1] the optimum total dose of penicillin and the proper time-dose relationship have not been satisfactorily established. The relative efficacy of penicillin and of arsenicals in the treatment of congenital syphilis has likewise not yet been determined. This report presents the results of treatment with penicillin in 22 cases of early congenital syphilis. The principal factors which are known to influence the treatment of this condition, such as the duration of the infection, the dosage of penicillin and the methods of administration, are also considered.

CASE MATERIAL AND PROCEDURES

All the children in this study were less than 17 months of age at the beginning of treatment, and none had received previous antisyphilitic therapy. Each child showed manifest syphilitic lesions of the skin and/or long bones in addition to a positive serologic reaction. The diagnosis of syphilis in every case was regarded as established beyond reasonable doubt.

At the beginning of this study, total doses of 40,000 to 50,000 units of penicillin per kilogram of body weight were employed. This dose corresponded to the total dose of 2,400,000 units, which had been found to be effective for adults with early acquired syphilis. With the appearance of failures in treatment in

From the Departments of Medicine and Pediatrics of the Grady Hospital, and Emory University School of Medicine and the Clinic for Genitoinfectious Diseases of the Georgia Department of Public Health.

The penicillin was provided by the Office of Scientific Research and Development from supplies assigned by the Committee on Medical Research for clinical investigations recommended by the Committee on Chemotherapeutic and Other Agents of the National Research Council.

1. (*a*) Lentz, J. W.; Ingraham, N. R., Jr.; Beerman, H., and Stokes, J. H.: Penicillin in the Prevention and Treatment of Congenital Syphilis, J. A. M. A. **126**:408 (Oct. 14) 1944. (*b*) Platou, R. V; Hill, A. J.; Ingraham, N. R.; Goodwin, M. S.; Wilkinson, E. E., and Hansen, A. E.: Penicillin in the Treatment of Infantile Congenital Syphilis: A Brief Preliminary Note, ibid. **127**:582 (March 10) 1945.

this series, the total amount of penicillin was increased to 60,000 to 70,000 units per kilogram. Sodium penicillin dissolved in isotonic solution of sodium chloride was given intramuscularly every three hours for sixty doses within a period of seven and one-half days. Fourteen patients received gradually increasing amounts of penicillin during the first to the third day, while the remaining 8 patients received equally divided doses. No further antisyphilitic treatment was given, and serologic tests were made at monthly intervals thereafter. All the cases were followed from nine to eighteen months. Examinations of the spinal fluid were not usually done until the end of the observation period. Roentgenograms of the long bones were taken at regular intervals following treatment.

RESULTS

Reactions.—Herxheimer reactions occurred during treatment in 12 of the 22 children. These usually appeared within twenty-four hours after the beginning of therapy and were manifested by an elevation of temperature, varying from 100 to 104 F. This increase in temperature seldom persisted for more than a day. It did not appear to be injurious to the child, and administration of penicillin was continued without interruption in all cases. For 4 of these patients the amount of penicillin given in each injection was not changed during the course of treatment. In the remaining 8 patients reactions developed despite the administration of gradually increasing amounts of the drug.

A slight rise in serologic titer appeared in 6 patients during the course of administration of penicillin. This transient increase in reagin has also been noted in adults and is another manifestation of the Herxheimer reaction. No other reactions to treatment were observed.

Clinical Response.—In all the patients with cutaneous and mucosal lesions, there was an immediate response to penicillin, and healing of the lesions was often complete by the end of the course of treatment. In the majority of instances clinical improvement of the osseous lesions was prompt, with some relief of the pseudoparalysis and of the tenderness on motion. Roentgenographic examination showed a slight improvement of the osseous lesions immediately following treatment in several cases, but in most cases complete healing of the syphilitic osteochondritis did not occur for two to three months after penicillin therapy. Although improvement of osseous syphilis may take place spontaneously, it is our impression that healing of these lesions occurs more rapidly following administration of penicillin. Examinations of spinal fluid were not done in all cases at the onset of treatment, but we have observed isolated instances of rapid reversal of initially positive spinal fluids.

Serologic Reversal.—Serologic reactions of the blood for syphilis have become negative in 13 of the 22 patients. All but 1 of these 13 children were less than 4 months of age at the start of treatment. Six of them had received 40,000 to 50,000 units, while the remaining 7 were given 60,000 to 70,000 Oxford units of penicillin per kilogram of body weight. Twelve of the 13 patients have been followed for eleven to eighteen months, while 1 patient has been observed for nine months. All of them are physically well and have normal spinal fluid.

The reversal of the serologic reaction usually occurred over a period of three to six months after the completion of penicillin therapy. The length of time necessary for the serologic reaction to revert to negative appeared to be directly related to the height of the initial quantitative titer. Several patients had a high initial Kahn titer, 360 units or more, and nine to ten months elapsed before their reactions became negative.

Serologic Relapse.—Serologic relapses developed in 2 of the 22 children. One of them, a 2 month old albino, was treated with 42,000 units of penicillin per kilogram of body weight. The quantitative Kahn titer had fallen from 400 to 80 units in six weeks, but five months later it had risen to 640 units. Examination of the spinal fluid at this time revealed 56 cells, 54 mg. of protein per hundred cubic centimeters and a positive reaction to the Wassermann test, with 0.125 cc. of fluid. The child had failed to gain weight and was irritable and poorly developed. Retreatment with double the original amount of penicillin was instituted. Five months later the serologic titer was 4 units, and the spinal fluid was normal. The patient had gained weight and now appears well.

The other patient who had serorelapses was 3 months old at the onset of treatment and had received 60,000 units of penicillin per kilogram of body weight. The cutaneous and osseous lesions healed promptly. The quantitative Kahn titer was 10 units at the onset of treatment but gradually rose to 640 units during the following six months The spinal fluid at that time contained 6 cells and 40 mg. per hundred cubic centimeters of protein and gave a positive reaction to the Wassermann test with 0.25 cc. of fluid on two examinations. There were no definite clinical signs of relapse. This patient was also re-treated with penicillin, but it is as yet too early to evaluate the results.

Seroresistance.—Four of the 22 children continue to show persistently positive serologic reactions of the blood sixteen months after penicillin treatment. In these patients the serologic titer is stationary at a low level or is very slowly declining. Each of these children was 4 months or older at the onset of treatment, and 2 were over 12 months

of age. All of these patients had been treated with 40,000 to 50,000 units of pencillin per kilogram of body weight.

All 4 children are well and have a normal spinal fluid. These patients have not been re-treated as yet, because a persistently positive serologic reaction has not been considered an indication in itself for further therapy.[1b] It is our opinion, however, that the majority of these patients will remain seropositive and that the results should be classified as unsatisfactory.

Deaths.—Three deaths occurred among the 22 patients. Two of the deaths occurred shortly after treatment. Both of the patients were small, severely infected premature infants, who were recognized as having an extremely poor prognosis. One of these was 3 days old at the onset of treatment, weighed 2,000 Gm. and showed extensive destruction of the long bones. The other infant was 1 month old and weighed 1,500 Gm. This child had severe jaundice and a papular eruption over the extremities. Both patients were treated with 60,000 units of penicillin per kilogram of body weight. In neither one did a Herxheimer reaction develop, and both seemed to tolerate penicillin therapy well. The younger child continued to lose weight after treatment; a severe diarrhea developed, and it died three weeks later. Roentgenograms at this time showed definite healing of the osseous lesions. The older infant was discharged after administration of penicillin in apparently good condition but returned three days later in a moribund state. The patient had had a severe diarrhea and had been vomiting for several days. He showed pronounced dehydration and jaundice and died on the following day. Autopsy revealed extensive syphilitic hepatitis with extreme disorganization and destruction of the hepatic parenchyma. There was considerable evidence of healing, however, and noticeable fibrosis had occurred. Healing syphilitic osteochondritis, interstitial pneumonia and questionable fibrosis of the spleen were also noted.

The third fatality was in a 4-month old child who died one and a half months after the completion of treatment with penicillin. This patient had received 60,000 units of penicillin per kilogram of body weight and showed a good response, with gain of weight, healing of osseous lesions and reduction of serologic titer. Five weeks after penicillin therapy the patient was readmitted to the hospital with a febrile illness, which was not thought to be related to her syphilitic infection. The child appeared seriously ill on admission, but seemed to improve after administration of sulfonamide compounds. She died unexpectedly, however, after one week in the hospital. Serologic tests for syphilis and examinations of spinal fluid had not been done, and an autopsy was not performed. Serologic tests on blood obtained after death showed

the same titer as the previous examination. It is impossible to state whether this patient's death was related in any way to syphilis or to the administration of penicillin.

COMMENT

In this series of 22 patients with congenital syphilis treated with penicillin, there were 2 with serologic relapse, 3 who died, and 4 with seroresistance. The remaining 13 children became clinically well and now have negative serologic reactions. These results are similar to those observed by Platou and his associates.[1b] who reported on 39 cases of infantile congenital syphilis studied in several different hospitals for four to twelve months. These workers gave smaller doses of penicillin, 16,000 to 32,000 units per kilogram of body weight, and found 5 instances of serorelapse, 9 instances of persistently positive serologic reactions and 25 cures. Five additional patients in their study died during or soon after treatment.

Although the results of our use of penicillin do not appear to be too encouraging, we believe that the ultimate outcome in these cases would not have been better had we used arsenicals and bismuth preparations. In a large series of patients treated with arsenicals, seroresistance, relapses and deaths were not uncommon.[2] It should be emphasized that deaths of children with congenital syphilis cannot be prevented by control of the infection alone. The majority of fatalities in this group of patients occur among the severely infected infants who are premature and malnourished. The widespread destruction of the liver found at autopsy in 1 of our patients is evidence of the overwhelming infection which these children may have. Even though healing of the syphilitic process occurs following treatment, the infant's condition may remain critical because of the extensiveness of the damage which has already occurred. The greatest factors in the prevention of deaths from congenital syphilis are adequate nutrition and hydration and the prevention of intercurrent infections.

Seroresistance in persons with congenital syphilis does not result from inadequate therapy alone. It is well known that the incidence of Wassermann-fast syphilis, both congenital and acquired, increases considerably when treatment is started late.[3] In this connection it should be noted that only the older children in this study showed persistently positive serologic reactions. It is unlikely. therefore, that routine chemotherapy would have appreciably reduced the number

2. Smith, F. R., Jr.: Congenital Syphilis in Children, Am. J. Syph. & Neurol. **19**:532, 1935.

3. Moore, J. E.: The Modern Treatment of Syphilis, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1941. Smith.[2]

of seroresistant patients in this series. The most effective means of decreasing the incidence of seroresistance is earlier diagnosis and treatment.

The optimum total dose and time-dose schedule of penicillin in the treatment of infantile congenital syphilis cannot be determined by study of a small series of cases. In view of the foregoing considerations, it is doubtful that doses of penicillin larger than those used in this study would result in fewer deaths. The effect of larger doses of penicillin on seroresistance is not known. We believe, however, that some modification of the present schedule for administration of penicillin will probably reduce the number of relapses. For this reason we are now giving a total dose of 100,000 units of penicillin per kilogram of body weight. This is given intramuscularly in equally divided doses every three hours for a period of ten days (see addendum).

The use of small doses of penicillin during the first few days of treatment did not appear to reduce the incidence or the severity of the Herxheimer reactions in our patients. Lentz and his associates [1a] have called attention to the possibility of therapeutic shock from too energetic treatment, but there was no evidence in this study that penicillin was injurious. Since adverse reactions to penicillin have been reported, however, the possibility of their occurrence should be kept in mind, particularly in the treatment of an acutely ill infant.

Quantitative serologic tests were found to be necessary in our follow-up study, for negative serologic reactions were not observed in either of our 2 patients with relapsing syphilis. The diagnosis of serorelapse in these children was based on the persistent rise in serologic titer and could not have been made if quantitative tests had not been done. The presence of positive spinal fluids in both of these cases is also noteworthy. An early diagnosis of serologic relapse may often be difficult because of variations in sensitivity to laboratory tests. It would seem advisable, therefore, in certain instances to repeat the examination of the spinal fluid during the period of observation and determine whether involvement of the nervous system is the cause of a persistently positive serologic reaction of the blood.

Our experience with penicillin in the treatment of infantile congenital syphilis leads us to believe that this drug is at least as effective as bismuth preparations and arsenicals. Moreover, it has added advantages in that it is nontoxic and does not required a prolonged course of treatment.

SUMMARY

Twenty-two children with infantile congenital syphilis were treated with penicillin and followed from seven to eighteen months. Thirteen of these patients are now clinically well, have negative serologic reactions

for syphilis and have normal spinal fluids. Four others show persistently positive serologic reactions of the blood sixteen months after treatment. These patients are also well and have normal spinal fluid. There were 3 deaths in this series and 2 instances of serologic and spinal fluid relapses. The deaths occurred in the more severely infected group, and seroresistance was found chiefly in the older children. Penicillin appears to be an effective agent in the treatment of congenital syphilis. It is most effective, however, when its use is combined with early diagnosis and adequate pediatric care.

ADDENDUM

The results which have been presented in this paper must be interpreted in the light of the fact that commercial penicillin has been a changing mixture of various substances. The content of "impurities" has gradually decreased as potency in terms of units per miligram has increased. The relative amounts of the several identified penicillin fractions, G, F, X and K, have likewise varied from time to time. Those two changes, and perhaps others, suggest that therapeutic efficacy may not have remained constant and that it may be significantly different today than it was originally. It is not now possible to assess the extent to which these changes may have affected the results here reported.

For these reasons, it seems advisable that the dose of penicillin recommended in this report should be at least doubled in order to maintain its efficacy in the treatment of infantile congenital syphilis.

Grady Hospital.
311 Doctor's Building.

Case Reports

SARCOIDOSIS (BESNIER-BOECK-SCHAUMANN'S DISEASE)

Report of a Case in a Child Simulating Still's Disease

AGUSTIN CASTELLANOS, M.D., F.A.A.P.
and
ENRIQUE GALAN, M.D.
HABANA, CUBA

SARCOID was formerly described in the textbooks of dermatology as a tumor-like or nodular formation usually located in the layers of the subcutaneous tissue of the face, the extensor surfaces of the arms and the trunk, showing a dark red, violaceous or brownish discoloration of the skin and not undergoing necrosis or ulceration but sometimes leaving an atrophic scar of the epidermis.[1]

In 1910, Darier[2] described four types of sarcoids. (*a*) Boeck's multiple benign sarcoid, or miliary lupoid; (*b*) subcutaneous sarcoid of Darier-Roussy, (*c*) indurated erythematous sarcoid of the extremities, and (*d*) Spiegler-Fendt sarcoid. The second type is localized to the hypodermis and shows a tendency to undergo necrosis or ulceration. It is considered a true nodular tuberculosis of the skin. The third type is a condition related to Bazin's erythema, which is also included among the exanthematous forms of cutaneous tuberculosis. The last type was also found not to be a true sarcoid but to consist of different and unrelated nodular infiltrations of the skin, such as leukemia cutis, sarcomatosis and lymphogranulomatosis.

Within the type known as Boeck's sarcoid[3] three subtypes are described according to their dermatologic aspect: (*a*) discrete nodular form, (*b*) large nodular form and (*c*) diffuse infiltrating plaquelike form. An erythrodermic form of sarcoid was chiefly reported in Scandinavian countries.[4] Sarcoids present a great variety of elemen-

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This case was discussed by the staff of the Children's Hospital of Habana at meetings 261 and 268.

From the Children's Hospital of Habana and Habana University School of Medicine, Chair of Pediatrics (Prof. A. Aballí).

1. Pardo-Castello, V.: Text-Book of Dermatology and Syphilology, Habana, Cuba, University of Habana, 1941, pp. 592-598.

2. Darier, J.: Compendio de dermatologia, Barcelona, P. Salvat, 1935, pp. 285-291 and 300-307.

3. Boeck, C.: Multiple Benign Sarcoid of Skin, J. Cutan. & Genito-Urin. Dis. **17**:543, 1899.

4. Andrews, G. C.: Diseases of the Skin, Philadelphia, W. B. Saunders Company, 1938.

tary cutaneous lesions, such as macules, amnuli, papules, nodules, plaques and tumors.

Several names were used to designate this condition: Boeck's sarcoid or benign miliary lupoid, benign lymphogranulomatosis (Schaumann),[4a] *maladie de Besnier-Boeck,* Hutchinson-Boeck's disease, osteitis tuberculosa multiplex cystica (Jüngling) and Mortimer's disease (Hutchinson). Since the time of William Osler's[5] original description of erythemas, many strictly considered dermatologic concepts of cutaneous eruptions claimed the attention of the internist, and it was soon found that some of them were not exclusively within the field of the specialist but were true systemic diseases involving any part of the organism.

Schaumann,[6] in 1914, reported that sarcoid might involve any organ with or without cutaneous lesions. At the Dermatologic Congress[7] held in Strasbourg in 1934 Pautrier[8] proposed the term "sarcoidosis" to be applied to a reticuloendotheliosis showing a common histologic structure of epithelioid cells in a granulomatous arrangement.

Sarcoidosis is characterized by a very slow onset, a protracted course and a protean symptomatology. It is a widespread disease of uncertain cause, commonly but not always associated with or complicated by tuberculosis. It may involve any part of the organism, but the lungs, lymph nodes, skin, eyes, bones, parotid glands and spleen are affected in most cases. The clinical diagnosis is a tentative one and has to be confirmed by the microscopic examination of biopsy specimens taken from any superficial structure of the body. The microscopic picture is that of a granuloma with or without multinucleated giant cells, formed by layers of epithelioid cells, surrounded by plasma, lymphocytes and round cells and more or less sharply demarcated from the neighboring tissues. This structure neither undergoes necrosis or caseation nor shows tubercle bacilli on proper staining.

In the lungs a miliary-like mottling seems to be the most frequent roentgenologic aspect in the early stage of the disease. It is sometimes followed by changes of a linear, strandlike character along the distribution of the bronchovascular ramifications. Functional symptoms like coughing, expectoration and dyspnea are out of proportion to the out-

4a. Schaumann, J.: Benign Lymphogranuloma and Its Cutaneous Manifestations, Brit. J. Dermat. **36**:515, 1924.

5. Osler, W.: On the Surgical Importance of the Visceral Crises in the Erythema Group of Skin Diseases, Am. J. M. Sc. **127**:751, 1904.

6. Schaumann, J.: Etude sur le lupus pernio et ses rapports avec les sarcoïdes et la tuberculose, Ann. de dermat. et syph. **6**:357, 1916-1917.

7. Réunion dermatologique de Strasbourg, Bull. Soc. franç. de dermat. et syph. **41**: 994-1392, 1934.

8. Pautrier, L. M.: La maladie de Besnier-Boeck, Presse méd. **43**:146, 1935.

standing lesions seen in the roentgenogram. The lymph nodes are usually enlarged but show no typical aspect whatsoever. Cutaneous manifestations are not an essential part of the disease, but different types, as previously mentioned, have been reported. The diffuse type shows a symmetric distribution involving the face, cheeks, nose, neck, chest and upper and lower limbs (on the extensor surface). There may be small brownish red nodules and small telangiectases. Complete healing without ulceration and healing with pigmented scars are the two usual alternatives in the evolution of cutaneous manifestation. Spina ventosa, diffuse osteitis and Jüngling's cystic osteitis [9] are the osseous lesions reported in sarcoidosis, the small bones (phalanges) being more commonly affected. Subjective symptoms are usually absent. According to Reisner,[10] the process does not extend into the joints, and therefore there is no limitation of function. Lesions of the eyes have been reported by Longcope,[11] Thornhill [12] and others. They are frequently localized in the uveal tract (iridocyclitis), cornea, conjunctiva and lacrimal glands. Mikulicz' syndrome and the uveoparotitis of Heerfordt [13] are also included within the clinical polymorphism of sarcoidosis. The spleen and liver are enlarged in some cases. Among other sites of involvement the peripheral muscles, the heart and pericardium, the meninges, optic nerve, pituitary gland, serous membranes, mammary glands, tendon sheaths and the mesenteric lymph nodes (some cases of regional ileitis) are mentioned by Longcope,[11] Reisner [10] and Palmer.[14]

Sarcoidosis is rare in children. Roos [15] reported a case of its occurrence in a 4 year old girl and mentioned 9 cases from the literature. Longcope [11] reported 1 case of sarcoidosis in a 14 year old Negro

9. Jüngling, O.: Osteitis tuberculosa multiplex cystica (Eine eigenartige Form der Knochentuberculose), Fortschr. a. d. Geb. d. Röntgenstrahlen **27**:375, 1920.

10. Reisner, D.: Boeck's Sarcoid and Systemic Sarcoidosis (Besnier-Boeck-Schaumann Disease): A Study of Thirty-Five Cases, Am. Rev. Tuberc. **49**:289 and 437, 1944.

11. Longcope, W. T., and Pierson, J. W.: Boeck's Sarcoid (Sarcoidosis), Bull. Johns Hopkins Hosp. **60**:223, 1937.

12. Thornhill, P. S., and Thornhill, E. H.: Boeck's Sarcoid with Nodular Iritis in a Child, Am. J. Dis. Child. **64**:262 (Aug.) 1942.

13. Heerfordt, C. F.: Ueber eine Febris uveo-parotidea subchronica an der Glandula parotis und der Uvea des Auges lokalisiert und häufig mit Paresen cerebrospinaler Nerven kompliziert, Arch. f. Ophth. **70**:254, 1909.

14. Palmer, J. H.: Boeck's Disease (Sarcoid): Its Clinical Groups and Diagnosis, Canad. M. A. J. **43**:11, 1940.

15. Roos, B.: Ueber das Vorkommen der Schaumannschen benignen Lymphogranulomatose (des Boeckschen benignen Miliarlupoids) bei Kindern, Ztschr. f. Kinderh. **59**:280, 1937.

boy (case 8). Two cases were reported by Naumann,[16] 1 by Müller[17] and 1 by Newns and Hardwick.[18] Thornhill[12] described nodular iritis in a 9 year old Negro girl. Posner[19] reported on a 25 month old girl with diabetes insipidus, anemia, thrombopenia and lesions in the large bones. Among the 35 patients of Reisner[10] there were 2 between the ages of 8 and 9 and 3 between 14 and 16. Our case is the first case of sarcoidosis observed at the Children's Hospital of Habana.

REPORT OF CASE

History.—S. B. P. a 6 year old white Cuban boy, entered the Children's Hospital of Habana, March 23, 1944, with the chief complaints of fever, polyarthritis and a symmetric erythematomacular eruption of the face and arms of three years' duration. His illness started in 1941 with a difficult gait on account of painful swelling of both ankles, associated with general malaise and pronounced asthenia. Three months later the joints of both wrists and elbows were also involved. The clinical picture remained stationary for one year, with occasional fever, after which both knee joints became swollen and showed the same clinical characteristics as the joints previously involved. There were a great enlargement of the joints and increased local temperature, but there was no red discoloration of the skin. The progressive involvement of the joints was always symmetric, and the general appearance was similar to that described in Still's disease. Erythema of the face, shoulders and arms was first noticed in 1943. The child did not lose any weight, and his condition was fairly good even though he had been always somewhat poorly nourished and underdeveloped. Symptoms of bronchitis with a dry cough had been occasionally present during the course of the disease. Because of the chronic swelling of the joints, the patient was brought to the outpatient department of the orthopedic clinic and then transferred to the pediatric ward.

Previous History, Development and Nutrition.—He was a full term baby, who had a normal delivery, weighing at birth 7½ pounds (3,400 Gm.). There were no birth injuries. The patient was a normal and healthy child up to the third year of age. He had been underfed and did not have milk or eggs for a long time because of the poor economic condition of the family. Examination of stools showed ova of Trichuris trichiura (whipworm) and Ascaris lumbricoides (roundworm) as well as the cystic form of Giardia intestinalis. No diseases, contagious or otherwise, are recorded in the clinical history.

Familial History.—There was no previous history of syphilis in the family. The child's grandmother had died of tuberculosis a long time before, but there had been no contact of the patient with her. There were three other children in the family; they were healthy, and none of them had ever had any condition similar to that of our patient.

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16. Naumann, O.: Kasuistischer Beitrag zur Kenntnis der Schaumannschen "benignen Granulomatose" (Morbus Besnier-Boeck-Schaumann), Ztschr. f. Kinderh. **60**:1, 1938.

17. Müller, R. W.: Ueber das generalisierte Miliarlupoid beim Kind, Monatschr. f. Kinderh. **72**:34, 1938.

18. Newns, G. H., and Hardwick, C.: Besnier-Boeck's Disease in an Infant, Arch. Dis. Childhood **14**:78, 1939.

19. Posner, I.: Sarcoidosis: Case Report, J. Pediat. **20**:486, 1942.

Physical Examination.—The child's weight was 28 pounds (12.7 Kg.) and his height 39 inches (99 cm.) (standards for his age: weight 45 pounds [20.4 Kg.], height 43½ inches [109.2 cm.]). His temperature (axilla) was 37.5 C. (99.5 F.), pulse rate 80, respiration rate 18 and blood pressure 90 systolic and 65 diastolic. The patient had showed a difficult and slow gait because of involvement of the large joints and kept his body stiff without flexion of the knees and elbows while walking. The skin of the cheeks, shoulders and arms showed areas of symmetric erythema, with moderate brownish red pigmentation and atrophy of the follicles, as well as scattered telangiectases. On both forearms and legs there was a definite violaceous netlike passive erythema with the typical characteristics of a livedo reticularis. On palpation no tumor or nodule similar to Boeck's sarcoid was

Fig. 1.—Erythematomacular eruption of the skin of the face.

detectable. The eyes were somewhat exophthalmic, with hyperemic conjunctivas and a white pinpoint spotty nonvesicular keratitis. The pupils were extremely contracted without light reflex due to synechia of the iris with the neighboring tissues. Transient and recurrent internal strabismus was also observed. The uveal tract was involved by the process. The eyegrounds were normal. The boy had carious teeth and mild gingivitis. The dental formula was as follows:

$$\frac{\text{Mmcba}}{\text{Mmcba}} \,|\, \frac{\text{—bcmMM}}{\text{abc-M-}}$$

The veins of the neck and upper portion of the thorax were engorged. The lymph nodes of the groins, axillas, epitrochlear region and neck were enlarged—

Summary of Laboratory Examination Data

Blood Counts

Date	Hemoglobin, %	Red Blood Cells	White Blood Cells	Polymorphonuclears	Stab Forms	Lymphocytes	Monocytes	Eosinophils
3/28/44	70	3,400,000	13,000	40	2	48	7	3
4/15/44	70	3,960,000	13,000	55	3	38	2	2
5/27/44	80	4,500,000	12,000	37	20	41	2	0
6/ 5/44	80	4,700,000	10,000	42	2	46	8	0
10/21/44	80	4,800,000	10,000	49	3	36	10	2
11/ 9/44	75	4,600,000	13,000	47	3	32	10	2
1/20/45	70	4,480,000	16,500	60	7	23	7	3
3/ 8/45	90	5,000,000	13,500	60	6	24	8	2

Urinalysis (Addis Count)

Date	Diuresis, Cc.	Specific Gravity	Albumin, Mg./ 12 Hr.	Red Blood Cells	White Blood Cells	Casts
3/23/44	55	1.025	4	27,500	630,000	27,500
5/27/44	100	1.024	0	15,000	4,250,000	0

Blood Chemistry

Date	CO_2 Vol.%	Glucose, Mg./ 100 Cc.	Protein Total, Gm./ 100 Cc.	Albumin, Gm./ 100 Cc.	Globulin, Gm./ 100 Cc.	Urea, Mg./ 100 Cc.	Cholesterol, Mg./ 100 Cc.	Calcium, Mg./ 100 Cc.	Inorg. Phosphorus	Phosphatase Units	Chlorides, R. B. C. Plasma
6/18/44	..	..	....	....	....	47	...	13	4	7	
5/23/44	55	66	....	....	....	30	266	..	..	..	80/240
5/31/44	..	95	....	....	....	30	...	10	6	3	160/320
4/20/45	..	..	7.52	4.13	3.39						

Renal Function Tests

3/25/44	Phenolsulfonphthalein excretion (i. v.)	40% first hour
3/25/44	Blood urea clearance	50% of normal
5/10/44	Dilution and concentration	Normal

Stools

Ova of Trichuris trichiura and Ascaris lumbricoides
Cystic form of Giardia intestinalis
Culture negative for Salmonella, Shigella and Eberthella

Test for Syphilis

Reactions to the Mazzini, Kahn, Meinicke and Sellek-Frade tests: negative

Tuberculin Test (Mantoux)

Date	Dilution	Reaction
3/25/44	1:1,000 and 1:100	Negative at 48 hr.
4/10/44	1:1,000	Negative at 48 hr.
7/30/44	1:1,000	Positive 4+

Sedimentation Rate (Westergren)

3/24/44	32 mm. per hour
4/10/44	13 mm. per hour
10/22/44	48 mm. per hour

Congo Red Test (Harmon-Kernin)

43 micrograms at the fourth minute
37 micrograms at the sixtieth minute
Negative reaction for amyloid disease

Electrocardiogram	Normal
Orthodiagram	Normal
Trichina test (intradermal)	Negative

Summary of Laboratory Examination Data—Continued

Basal Metabolic Rate

3/11/44	+30%
7/ 4/44	+32%

Bacteriology and Cytology

4/15/44	Throat culture: Staphylococcus aureus Sputum (gavage): No acid-fast bacilli
5/ 8/44	Exudate from the knee joint (tap) Yellowish cloudy fluid with alkaline reaction Rivalta's test: 4+; protein, 4.1 Gm. per 100 cc. Total cells: 156,000 per cu. mm. Differential count: polymorphonuclear leukocytes, 63%; lymphocytes, 17%, and endothelial cells, 20% Direct smears: negative for micro-organisms Cultures on blood agar, chocolate agar, Brewer's and Guernon's (tubercle bacilli medium): no pathogenic organisms after forty days of observation Inoculations of rabbit and guinea pig: nothing abnormal revealed
10/16/44	Pleural effusion (tap) Rivalta's test: 4+; protein 4.3 Gm. per 100 cc. Differential count: lymphocytes 70%, polymorphonuclear leukocytes 20% and endothelial cells 10% Cultures and inoculations: nothing abnormal revealed

Roentgenograms

3/26/44	Lungs: Miliary-like mottling of both lungs; tuberculosis must be ruled out
4/ 5/44	Paranasal sinuses: Thickening of both maxillary mucosal sinuses
7/ 4/44	Bones and joints: Bone age of 4 years; increased volume of soft para-articular tissues; no lesion of large bones; no alterations of bones similar to those reported in the fingers (phalangeal bones) of persons with sarcoid
10/16/44	Chest: Pleural effusion on right hemithorax with displacement of mediastinal organs toward the left side
11/16/44	Chest: Atelectasis at the base of right lung and artificial pneumothorax on the same side, with partial collapse of the rest of the right lung
1/11/45	Chest: Total regression of atelectasis and disappearance of artificial pneumothorax; enlarged tracheobronchial lymph nodes; changes of strandlike character along the distribution of bronchovascular markings; visible lower interlobar fissure of the right lung

of the size of a walnut. They were firm, did not adhere to the surrounding tissues and were not painful on palpation or pressure. A persistent dry cough was noted, and typical signs of bronchitis (coarse and moist rales) were present in both lungs. The cardiovascular system was normal. The liver was within normal limits, but the spleen was definitely enlarged, reaching about 2½ fingerbreaths below the left costal margin. It was firm, with a smooth surface, and kept its normal anatomic configuration.

Most of the large joints were greatly enlarged. The ankles, knees, wrists, elbows and shoulders were extremely swollen. Slight limitations of extension and flexion movements were present, with increased local temperature but no red discoloration of the skin. On palpation there was a feeling of fluctuation due to increased accumulation of fluid, with bulging and thickening of the synovial membranes, this condition being responsible for the great deformity of the joints. Hard tissues, such as bone and cartilage, did not seem to be involved, and therefore synovitis rather than osteoarthritis was considered the strongest clinical possibility. Both patellas were slightly displaced toward the inner side of the knees on account of the considerable bulging of the synovial membranes. The small joints were not involved in the process. The fingers and toes showed a normal configuration and spindle-shaped or spina ventosa deformity was not present.

The rest of the examination showed normal conditions.

Pathologic Report.—Cytodiagnostic Puncture of the Lung and Aspiration of Sternal Marrow: The diagnostic tapping of the right lung was performed at the beginning of the observation when the lung was seen to have the miliary-like mottling on roentgenologic examination (June 10, 1944). The importance of the diagnostic puncture of the lung in lipid pneumonia has been stressed by one of us.[20] The sternal puncture was done later according to the technic advised by Dressler.[21] The aspirated blood was allowed to clot and was then embedded in paraffin and subsequently treated as any tissue section for histologic examination.

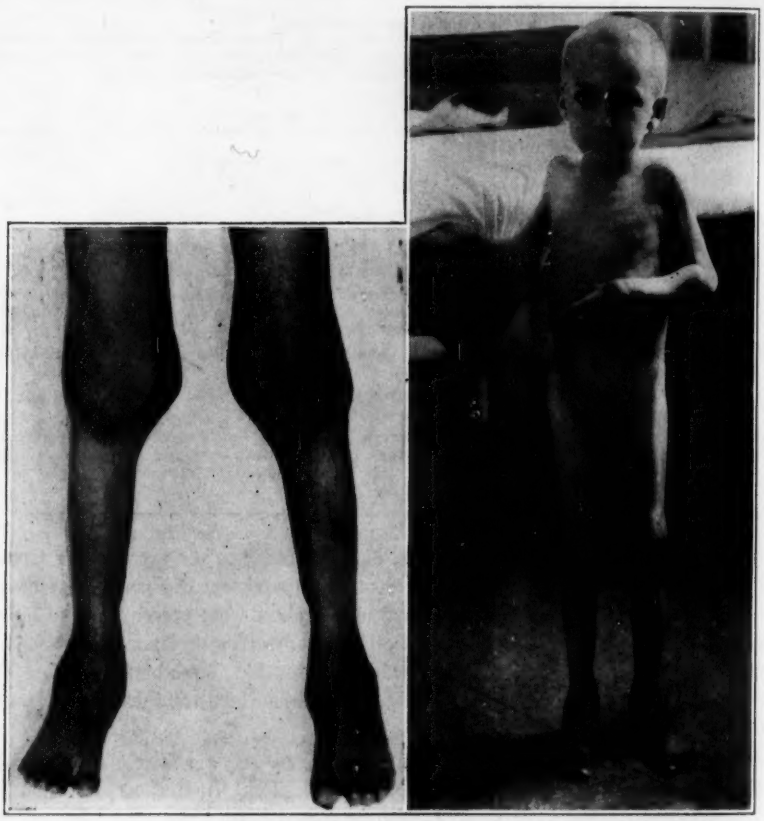

Fig. 2.—Enlargement of the joints.

In the material aspirated from the lung, numerous cells were found which showed the characteristics of histiocytes. They were large-sized cells with two to four poorly stained nuclei peripherally located on a basophilic cytoplasm (Giemsa

20. Castellanos Gonzalez, A.; Pereiras, R.; Valdés Díaz, R., and Sánchez Santiago, B.: Bronconeumonias crónicas aspirativas con especial referencia a las lacteas: importancia del neumograma en el diagnóstico intra-vitam, Arch. de med. inf. **12**:191, 1943.

21. Dressler, M.: Ueber einen Fall von Splenomegalie, durch Sternalpunktion als Boecksche Krankheit verifiziert, Klin. Wchnschr. **17**:1467, 1938.

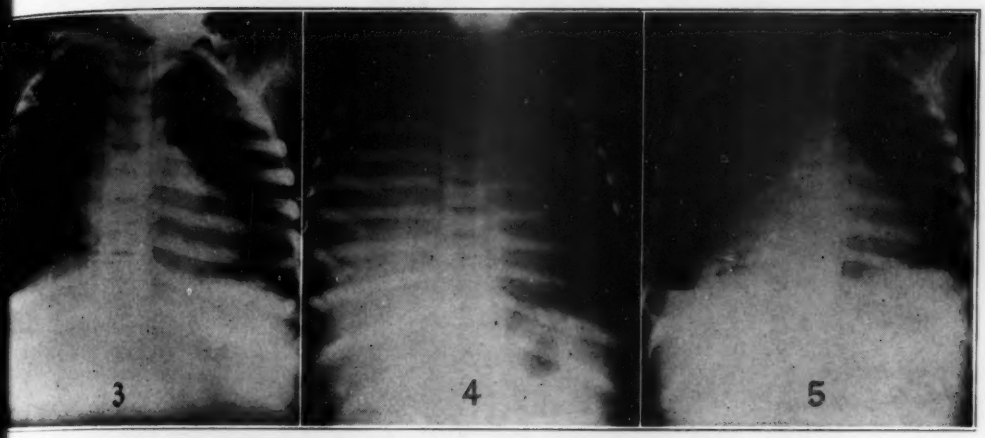

Fig. 3.—Miliary-like mottling of the lungs. No enlarged lymph nodes. Negative reaction to a tuberculin test up to a 1 : 100 dilution (March 26, 1944).

Fig. 4.—Fibrinous pleurisy. A strongly positive reaction to a tuberculin test (July 30, 1944).

Fig. 5.—Artificial diagnostic pneumothorax after tapping of the lung and aspiration of pleural effusion. Partial collapse of the middle and upper lobes. Pneumonic process of the lower portion of the middle lobe. Enlarged right paratracheal lymph node.

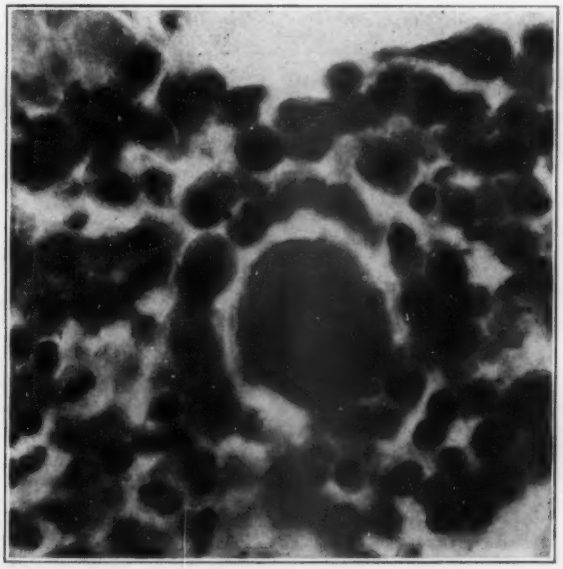

Fig. 6.—Multinucleated giant cell seen on a Giemsa-stained smear from the sternal bone marrow. The cell shows seven poorly stained nuclei in a ringlike disposition on a deeply eosinophilic cytoplasm. Histiocytes, round cells, lymphocytes and a few eosinophils and polymorphonuclear leukocytes form a lymphogranulomatous infiltration around the giant cell.

stain). Other cells, such as lymphocytes, plasma cells and polymorphonuclear leukocytes, were also present.

The material from the bone marrow contained multinucleated giant cells similar to those found in sarcoid granuloma. They showed from 7 to 20 nuclei of

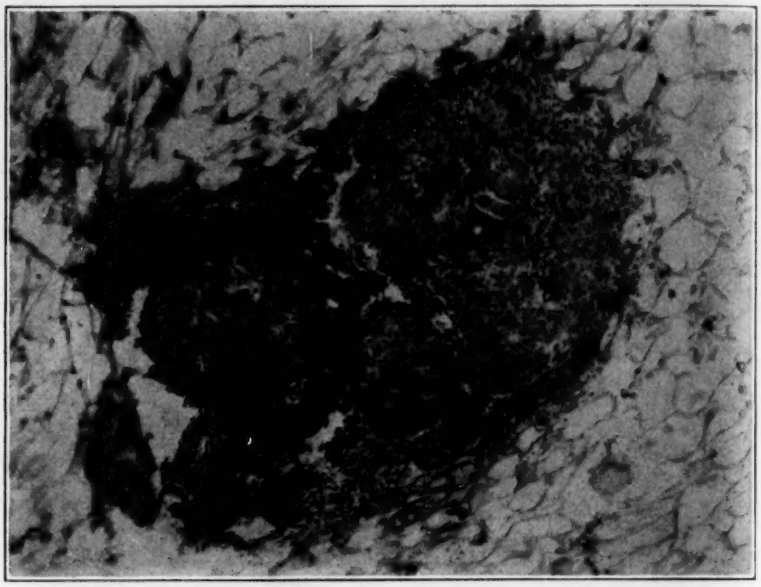

Fig. 7.—Three sarcoid granulomas located in the subcutaneous fatty tissue.

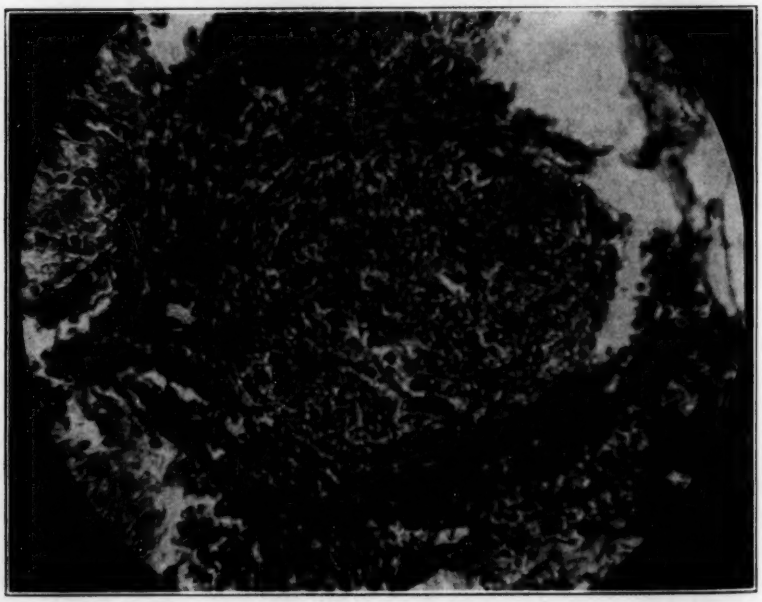

Fig. 8.—Enlarged view of one of the granulomas seen in figure 7.

distinctly different microscopic appearance from that of the nuclei of megakaryocytes, as they were independent of each other, without any chromatin threadlike

Fig. 9.—Sarcoid granuloma located in the deltoid muscle.

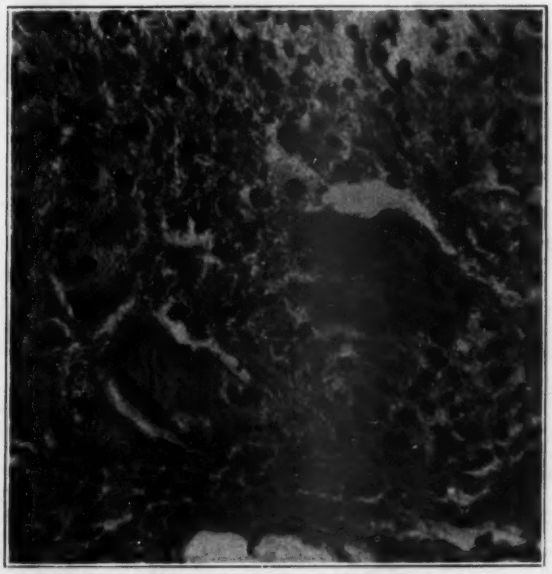

Fig. 10.—Enlarged view of the giant cells seen in figure 9.

connection, poorly stained and peripherally located on a deeply eosinophilic cytoplasm. No tubercle bacilli were seen in smears either from the lung or from

bone marrow after Ziehl-Neelsen staining. This observation was not sufficient to make a diagnosis of Boeck's disease as no typical histologic structure was observed. However, in the case reported by Dressler [21] the material aspirated

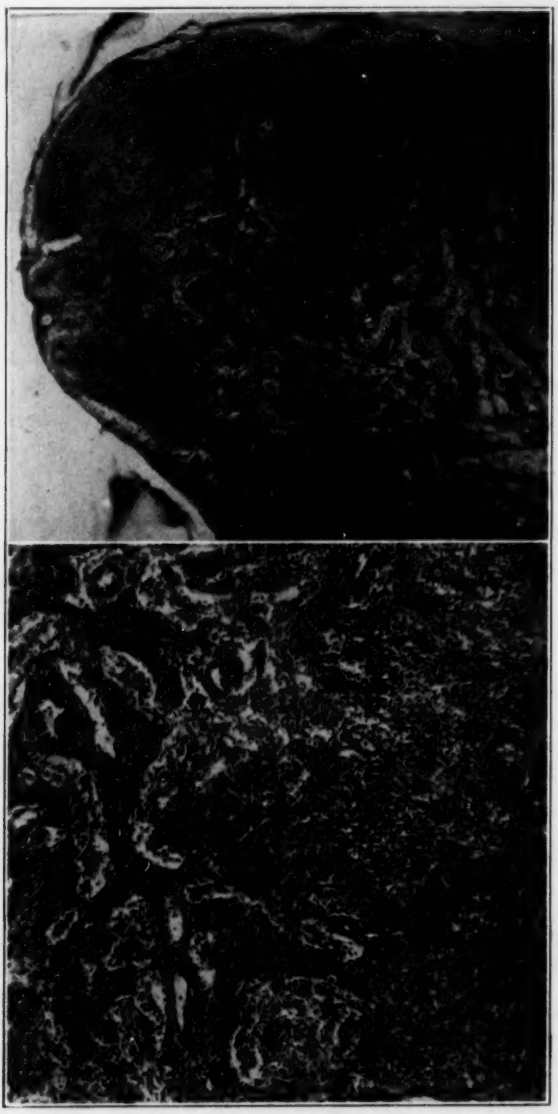

Fig. 11.—Panoramic and enlarged views of the lymph node from the right inguinal region. There is a complete substitution of the normal histologic structure by a diffuse infiltration of epithelioid cells.

from the sternal bone marrow showed typical sarcoid granulomas. This patient had an enlarged spleen for three years without any other clinical manifestation except increased bronchovascular markings of the lungs.

Biopsies: Skin, subcutaneous tissue and muscle were taken from the left deltoid region on June 20, 1944 and stained with hematoxylin and eosin and Van Gieson and Ziehl-Neelsen stains or acid-fast bacilli. There was a slight atrophy of the epidermis. In the subcutaneous and muscular tissues, six to ten nodular structures were present which showed the microscopic aspect of sarcoid ganulomas. They were formed by epithelioid cells more or less sharply demarcated from the surrounding tissues by a thin layer of plasma cells, lymphocytes and histiocytes. These cells were located in a loose connective tissue simulating a capsular structure. At the center of some of these nodular formations, there were multinucleated giant cells with ten to twenty nuclei arranged as in the tuberculous Langhans cell. The nuclei were irregularly distributed and mostly clumped at the center of the cytoplasm of other giant cells present in the same granuloma. There were no caseating or necrotizing changes in the granulomata, but hyalinization was present in a few of them. No tubercle bacilli were found.

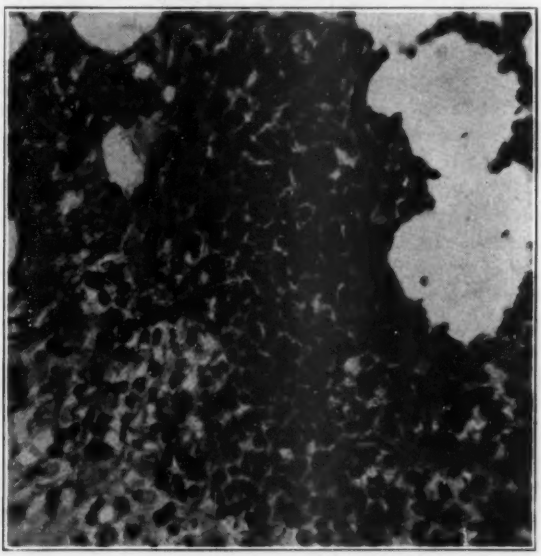

Fig. 12.—Biopsy of synovial membrane. Chronic nonspecific inflammatory process. Hemorrhage and neoformation of capillary blood vessels.

A lymph node from the right inguinal region was removed on Oct. 21, 1944 and stained with hematoxylin and eosin and Van Gieson and Ziehl-Neelsen stains for acid-fast bacilli. A panoramic view of the lymph node showed a complete transformation of the normal histologic structure into a diffuse infiltration of epithelioid cells, which in some places acquired nodular configuration. Two of these nodular structures showed hyaline degeneration. The histologic appearance of the lymph nodes was characteristic of a reticuloendotheliosis. There were numerous binucleated histiocytes in amitotic division with macrophagic activity and deposition of pigment.

A small section of synovial membrane was removed from the left knee on April 20, 1945 and stained with hematoxylin and eosin and Van Gieson and Ziehl-Neelsen stains for acid-fast bacilli. The synovial membrane showed the histologic structure of a chronic nonspecific inflammatory process characterized by: neoformation of capillary blood vessels, congestion and hemorrhage, edema and fibrinoid degeneration

of the wall of the small arteries, clumps of plasma cells with histiocytes, lymphocytes and a few mononuclear eosinophils and polymorphonuclear leukocytes. Even though the microscopic appearance of the cellular infiltration in the synovial membrane did not show any granulomatous structure it was also quite different from the pathologic changes usually observed in tuberculous arthritis. Therefore, in the absence of clinical and pathologic evidences of any other etiologic factor responsible for the chronic nonspecific inflammatory process of the joints, it must be provisionally accepted as due to sarcoidosis until further observations confirm or deny this point of view.

Clinical Course.—The child was kept in the hospital from March 23 to July 29, 1944 and from Oct. 4, 1944 to May 30, 1945. His condition was fairly good, but he did not look very active. His temperature was irregular, but it was never higher than 38.5 C. (101.5 F.), axillary. On two occasions there was a mild *poussé* of arthritis, with painful swelling of the large joints and increased local temperature. Infected teeth were removed, and gingivitis was locally treated. He received 3 Gm. of sulfanilamide daily for a month without any definite improvement. A whole blood transfusion was given, and he was discharged with the diagnosis of either tuberculous or chronic polyarthritis with splenomegaly (Still's disease). Treatment with calcium gluconate and copper morrhuate injections, proper feeding and adequate intake of vitamins and rest were ordered to be followed at home.

Four months later he was brought to the hospital for the second time with dyspnea, remittent fever and great loss of weight. His condition was poor, and on physical examination dulness, expiratory bronchial breathing and fine moist râles at the base of the right lung were noted. The joints were extremely swollen and the cutaneous lesion was prominent. The spleen was still enlarged and there was a definite involvement of the uveal tract with haziness of the cornea. The roentgenologic examination revealed a pleural effusion. At this time the tuberculin test at 1: 1,000 dilution, gave a strongly positive reaction and atypical Arthus phenomenon developed. Bacteriologic examination (cultures and inoculations) of the pleural effusion, joint exudate and sputum did not yield tubercle bacilli or any pyogenic micro-organism. The pleural effusion was aspirated and an artificial pneumothorax was performed, visualizing a zone of pneumonic process at the base of the right lung and an enlarged right mediastinal lymph node. The roentgenogram of the phalanges did not show any osseus changes like those described in sarcoidosis. Biopsies of the skin and subcutaneous and muscular tissues from the deltoid region as well as a lymph node removed from the right inguinal region showed the typical microscopic picture of sarcoidosis.

NOTE.—After the paper was submitted for publication, Pott's abscess of the dorsal spine, developed, and the child died later from tuberculous meningitis secondary to this abscess. An autopsy was not allowed.

COMMENT

This case was previously discussed at two roentgenologic conferences because of the peculiar miliary-like mottling of both lungs, closely resembling tuberculosis. However, the roentgenologic aspect of the *granité* was thinner than that usually observed in miliary tuberculosis. At this time there were no enlarged mediastinal lymph nodes and reaction to the tuberculin test was absolutely negative up to 1: 100 dilution.

Other diseases which may determine a miliary mottling on the roentgenogram, as carcinomatosis, silicosis, Hodgkin's disease, bronchopneumonia and periarteritis nodosa, were ruled out because of the protracted course of the condition and the absence of clinical evidence. A clinical syndrome characterized by prolonged fever, polyarthritis, splenomegaly, bizarre cutaneous eruption, serositis and myositis, has been reported in more or less definite clinical entities, formerly grouped by Osler [5] as cutaneous diseases with visceral manifestations and recently included under the heading of visceral angiitis by Dock [22] and vascular allergy by Harkavy.[23]

The chronic and great enlargement of the joints in this child was quite different from the acute episodes of arthritis seen in that group of diseases. Thus, three possibilities were considered at the very beginning in our case: (*a*) infectious arthritis, (*b*) the form of tuberculous rheumatism described by Poncet and (*c*) Still's disease. The purulent exudate found in the joints supported the diagnosis of infectious arthritis and ruled out momentarily the diagnosis of tuberculosis, but the bacteriologic investigations were negative for pyogenic microorganisms as well as for tubercle bacilli. The adequate treatment for both conditions was also unsuccessful. Therefore, Still's disease seemed the strongest diagnostic possibility. It is obvious that the association of chronic polyarthritis deformans, splenomegaly, cutaneous manifestations, enlarged lymph nodes and ocular lesions was evidence in favor of a systemic disease rather than of a simple arthritis.

The finding of granulomas formed by epithelioid and multinucleated giant cells which did not show tubercle bacilli aroused the suspicion of sarcoidosis. Syphilis, leprosy and trichinosis were ruled out by the corresponding investigation. Later the child had a fibrinous pleurisy and either pneumonia or a tuberculous lobitis of the lower lobe of the right lung. The reaction to the tuberculin test became strongly positive at a 1: 1,000 dilution and determined a typical necrotizing Arthus phenomenon. The miliary mottling disappeared and was followed by increased bronchovascular markings.

Fibrinous pleurisy seldom follows miliary tuberculosis in children. Furthermore, once the tuberculous miliary dissemination is established it is usually progressive, and death is the rule. This supported the diagnosis of sarcoidosis, even though a strongly positive reaction to a tuberculin test expressed a hyperergic stage of tuberculosis which might be responsible for the pleural effusion that was present at this time in our patient (Ranke's second stage).

22. Dock, W., cited by Krupp, M. A.: Urinary Sediment in Visceral Angiitis (Periarteritis Nodosa, Lupus Erythematosus, Libman-Sacks "Disease"), Arch. Int. Med. **71**:54 (Jan.) 1943.

23. Harkavy, J.: Vascular Allergy, Arch. Int. Med. **67**:709 (April) 1941.

The microscopic picture observed in the lymph node confirmed the diagnosis of sarcoidosis. So, just as the uveoparotitis of Heerfordt [13] and Mikulicz' disease have been reported as a part of the clinical picture of sarcoidosis, we may consider our patient as having, or simulating, Still's disease owing to the association of tuberculosis and sarcoidosis. Still's syndrome,[23a] or chronic symmetric polyarthritis with splenomegaly, is not a definite nosologic entity, since the cause and the pathologic changes are unknown. The same holds true, of course, for sarcoidosis, but this condition shows, at least, a common pathologic picture in any structure involved by the process. The relationship of tuberculosis and sarcoidosis is still under controversy, but the frequent association of the two diseases (40 per cent according to Kissmeyer [24] and Reisner [10]) seems more than coincidental.

SUMMARY

We have reported our first case of sarcoidosis, the disease occurring in a 6 year old white Cuban boy observed at the Children's Hospital of Habana.

The disease started when the child was 3 years old with a gradual onset, prolonged fever and chronic polyarthritis deformans, with splenomegaly, simulating Still's disease.

The clinical picture was also characterized by a miliary-like mottling of both lungs, enlarged mediastinal and peripheral lymph nodes, a symmetric erythematomacular cutaneous eruption on the cheeks, nose, shoulders and arms with brownish pigmentation and small telangiectases and atrophy of the epidermis. There was a livedo reticularis on the skin of the forearms and legs. Ocular manifestations were observed such as moderate exophthalmos, recurrent internal strabismus, congestion of the conjunctivas, a pinpoint nonvesicular keratitis with late descemetitis, involvement of the uveal tract and synechia of both irises.

Typical granulomas with or without multinucleated giant cells but formed by epithelioid cells like those reported in sarcoidosis were found in the subcutaneous tissue and peripheral muscle (deltoid).

A diffuse infiltration of epithelioid cells was observed in the lymph node with the characteristics of a reticuloendotheliosis.

Cytodiagnostic puncture of the lung and aspiration of sternal marrow yielded numerous histiocytes and multinucleated cells respectively, those found in the bone marrow being similar to the giant cells seen in sarcoid granuloma.

23a. Still, G. F.: On a Form of Chronic Joint Disease in Children, Med.-Chir. Tr., London **80**:47, 1896-1897.

24. Kissmeyer, cited by Longcope and Pierson.[11]

The involvement of the large joints in the form of a chronic polyarthritis deformans is an unusual feature in this case, and it was not reported in the literature consulted.

Biopsy of the synovial membrane showed a chronic nonspecific inflammatory process. Sarcoid granuloma was not found in this structure. In the absence of clinical and pathologic evidence of any other etiologic factor responsible for the chronic polyarthritis deformans we must provisionally accept it as due to sarcoidosis until further observations confirm or deny our point of view.

The condition was already complicated by tuberculosis, as indicated by a late strongly positive reaction to a tuberculin test, a fibrinous pleurisy and a pneumonic process of the lower lobe of the right lung similar to the so-called tuberculous lobitis.

Hospital de Infancia, F 27, Vedado.

CONGENITAL HEMIHYPERTROPHY

Report of a Case with Postmortem Observations

STANLEY J. RUGEL, M.D., PHILADELPHIA

IT IS not uncommon in pediatric practice to see examples of asymmetry involving parts of the face or even, at times, of the extremities. However, when this asymmetry affects a complete side and is found in the bone structure as well as in the soft tissues it is rare enough to report. The number of such cases described in the literature to date is still probably under the one hundred mark. These cases, described as instances of total (or complete) asymmetry, may be of the atrophic or hypertrophic type. The nature and especially the causation of this condition have never been satisfactorily explained, and this is so in no small measure because of the lack of autopsied material. In an article published in 1942, Schwartzman and others [1] stated that only 4 cases have come to postmortem examination. In the case we are about to report we were able to obtain complete postmortem studies.

REPORT OF CASE

E. H., a white girl, was first seen in December 1940, at the age of 6 months, because of noisy breathing and an abnormal appearance. Delivery had been by cesarean section, and at birth her attending physician noted certain differences in the two sides of the body.

On examination one was immediately struck by the asymmetry of the head and face (fig. 1 *A*) and then by the inequality of the lower extremities (fig. 1 *C*). The general impression was, as Gesell [2] has described, "a union into one organism of two different halves." The right side of the scalp exhibited a heavy growth of hair, whereas on the left side the hair appeared sparse (fig. 2). The head gave the impression of hydrocephalus, and the anterior fontanel, which was huge, was asymmetric. The remainder of the body shared in this inequality to a greater or less degree. A violet red hemangioma covered most of the left arm and another involved the upper lip. When the baby cried, a discoloration appeared and covered the whole left side of the face and trunk. It was interesting to observe also during the crying profuse sweating limited to the left side of the body.

The patient was admitted to the pediatric service of Dr. Robert Schless in the Jewish Hospital of Philadelphia on Dec. 29, 1940. Measurements of the body

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From the Pediatric Service of Dr. Robert Schless, Jewish Hospital.

1. Schwartzman, J.; Grossman, L., and Dragutsky, D.: True Total Hemihypertrophy: Case Report, Arch. Pediat. **59**:637, 1942.

2. Gesell, A.: Hemihypertrophy and Mental Defect, Arch. Neurol. & Psychiat. **6**:400 (Oct.) 1921.

were taken (table 1) and showed consistently different readings on the two sides. It is noteworthy and mentioned in the literature on this subject[3] that differences

Fig. 1.—*A*, facial asymmetry seen in profile view. *B*, facial asymmetry seen in full face view, also asymmetry of the vulva. *C*, asymmetry of the lower extremities, a marked difference being seen in the gluteal folds and in the girth of the legs.

in girth were more striking than differences in the length of the extremities. Laboratory data, including a Wassermann reaction of the blood and the blood levels of

3. Peabody, C. W.: Hemihypertrophy and Hemiatrophy: Congenital Total Unilateral Somatic Asymmetry, J. Bone & Joint Surg. **18**:466, 1936.

sugar, calcium, phosphorus, phosphatase and cholesterol, were all within normal limits. Roentgenologic study of the skull suggested hydrocephalus, and a roentgenogram of the chest disclosed an enlarged right thymic lobe. Roentgenograms of the lower extremities revealed a difference of 1 cm. in the lengths of the tibia and fibula on the two sides (fig. 3).

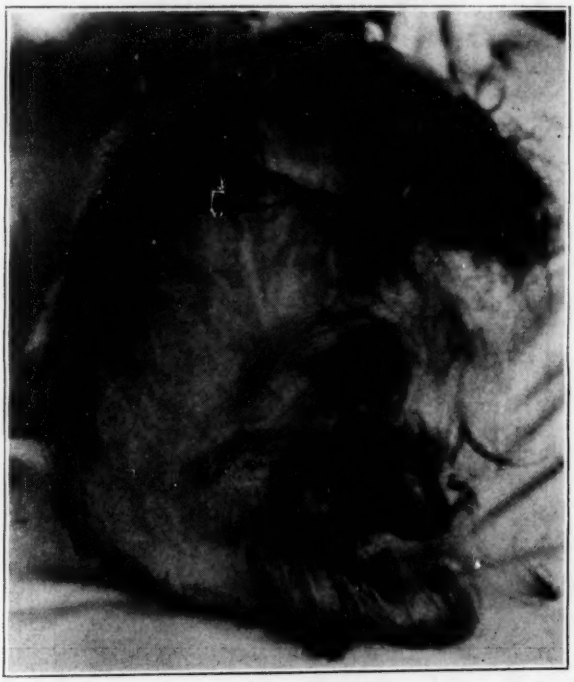

Fig. 2.—Different growth of hair on two sides of the scalp.

TABLE 1.—*Comparative Measurements During Life*

	Right Side, Cm.	Left Side, Cm.
Root of nose to external auditory meatus	10.5	9.5
Midline to angle of meatus	7.5	6.5
Circumference of wrists	10.5	9.75
Circumference of forearms	12.25	12.25
Circumference of arms	11.5	11.5
Circumference of thighs	22.0	18.5
Circumference of calves	17.0	15.5
Circumference of chest	21.0	20.0
Circumference of abdomen	22.0	21.5
Length of lower extremity	30.5	29.7
Length of upper extremity	22.5	21.0

After irradiation treatment of the thymus, an encephalogram was made. This study proved interesting for several reasons. In the first place, there was an obvious difference in the sizes of the two cerebral hemispheres, with a similar difference in the appearance of the subarachnoid air (fig. 4 *A*). In the second

Fig. 3.—Roentgenologic study shows not only a difference in the lengths of the tibia and the fibula on the two sides but also a difference in the soft tissues. (From the x-ray department of Dr. Leon Solis-Cohen, Jewish Hospital.)

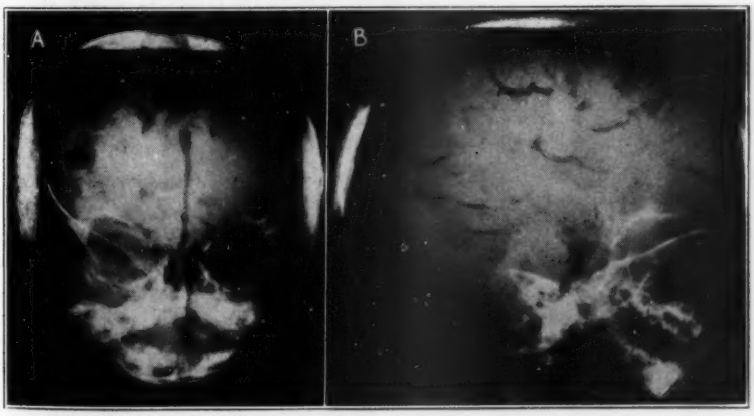

Fig. 4.—*A*, anteroposterior view of the encephalogram shows asymmetry of the two cerebral hemispheres, with a greater amount of subarachnoid air on the right side. (From the x-ray department of Dr. Leon Solis-Cohen, Jewish Hospital.) *B*, encephalogram, showing failure of air to enter the ventricular system. (From the x-ray department of Dr. Leon Solis-Cohen, Jewish Hospital.)

place, the ventricular system failed to show air, and this led the radiologist to make a diagnosis of cerebrospinal block with internal hydrocephalus (fig. 4*B*). The attending staff, with one or two exceptions, agreed with the diagnosis at admission, congenital total hemiatrophy of the left side. The possibility of a right-sided hemihypertrophy was considered but discarded because clinically the deviation from normal appeared greater on the left side. The presence of the striking vascular cutaneous defects on this side, the abnormal sweating response to crying and the lack of hair on this side influenced this decision.

The patient's course after discharge from the hospital was characterized by a noticeably retarded developmental pattern. Episodes of high fever with insufficient cause occurred frequently and could be attributed only to an unstable temperature control center. On Oct. 28 1942, when she was close to 2 years of age, the patient contracted an infection of the upper respiratory tract, which rapidly developed into an obstructive laryngitis. In spite of a tracheotomy, she died in the Philadelphia Hospital for Contagious Diseases on October 30.

TABLE 2.—*Comparative Measurements at Autopsy Table*

	Right, Cm.	Left, Cm.
Length of arms	23.5	22.0
Length of legs	34.0	31.5
Circumference of thighs	22.0	19.0
Adrenal glands	Equal size	
Kidneys	50.0 Gm.	45.0 Gm.
Tubes and ovaries	Equal size	
Circumference of skull	28.0	24.5
Cerebral hemispheres	19 × 10.5 × 8	19 × 6 × 6
Cerebellar hemispheres	Larger	Smaller
Cerebral peduncles, pons and midbrain	Equal size	
Lobes of thyroid gland	3 × 1.5	2 × 1.2

A complete autopsy was performed by Dr. A. R. Peale, who noted at the beginning that the entire right side of the body was definitely larger than the left. His comparative measurements and weights are recorded in table 2. It will be seen that certain paired organs, such as the kidneys, show differences in size, whereas others, such as the adrenal glands and the ovaries, do not. The most striking observation was bilateral enlargement of the brain, more pronounced on the right side. Dr. Peale noted that "the brain is considerably heavier than normal and weighs 1,670 Gm. It has the gross appearance of an adult brain. The convolutions are flattened throughout, although more so on the right side than on the left." Cut sections of the ventricular system failed to reveal any dilatation.

Comparative microscopic study, made by the pathologist, showed no difference in muscle sections taken from the right and left sides of the diaphragm. In studies of the skin, it was found that the corium from the right side was thicker than that from the left side. Microscopically, the brain showed pathologic changes consisting of extensive edema and congestion. "In some areas," Dr. Peale said in describing the condition, "the edema had gone on to appear as focal demyelinated areas. There is a very occasional patchy infiltration of cells around the smaller vessels, suggesting early acute encephalitis. Sections of the right half of the brain are more cellular than those of the left, the cells being chiefly of the glial supportive variety (microglial cells)."

COMMENT

Inasmuch as the postmortem examination revealed hypertrophy of the left cerebral hemisphere as well as of the right, though to a lesser degree, it might be argued that this was not a strictly unilateral total asymmetry. However, with more autopsy studies, this mixed picture might more often be found. In Gesell's survey [2] of recorded cases of hemihypertrophy, there are 3 cases of patients described as having enlargement of the cerebral hemisphere on the same side as the somatic enlargement. No mention is made of the opposite hemisphere, which apparently was normal. In Gordinier's case,[4] in which complete, or total, left-sided enlargement of the body was shown, there was definite symmetric enlargement of the whole left cerebral hemisphere. This hemisphere measured 1 cm. more in its anteroposterior diameter and 1.25 cm. more in its transverse diameter than the opposite one. The significance of this observation may affect etiologic theories based on the purely unilateral pattern of this condition.

The discrepancy in the clinical and roentgenologic diagnosis of cerebrospinal block and the pathologic observations calls for some explanation. The only one that suggests itself is that with greatly enlarged subarachnoid spaces insufficient air was injected and incomplete filling resulted.

The literature on the subject of hemihypertrophy is well supplied with speculative theories on etiology. A complete discussion of this interesting phase of this problem can be found in a recent paper by Schwartzman and others.[1] In spite of our fairly complete postmortem studies, my associates and I can make no positive contribution. Certain theories, such as congenital syphilis, vascular disease or disturbance of the lymphatic system, bear no relation to this case. Since by gross and microscopic studies the thyroid gland, pituitary gland, pancreas, thymus and adrenal glands were found normal, we could hardly support an endocrine theory. Gesell's twinning theory, of a union into one organism of two different halves, would seem to fit the picture of our patient superficially, but would hardly explain the overgrowth of the left cerebral hemisphere, with hypertrophy on the right side. By elimination, this would leave us with the most popularly held view, that hemihypertrophy is in some way tied up with an embryonic defect of the vegetative nervous system. This affects the trophic function of that system, and the result is a bizarre picture of hemihypertrophy.

4. Gordinier, H. C.: Case of Unilateral Hypertrophy of the Whole Left Side with Autopsy, Albany M. Ann. **39**:47, 1918.

SUMMARY

The case of hemihypertrophy described exhibited all the typical features of this condition—vascular cutaneous lesions, unilateral sweating, instability of temperature control, change in the hair and skin, cerebral abnormalities and the obvious inequality of the two sides. Postmortem study disclosed deviation from the accepted picture of purely unilateral asymmetry. The brain showed tremendous hypertrophy and significant histologic changes.

700 West Roosevelt Boulevard.

Progress in Pediatrics

RELATIONSHIP OF PEDIATRICS AND PSYCHIATRY

MILTON J. E. SENN, M.D.
NEW YORK

THE historical background of pediatrics in the United States in terms of mental hygiene is contrasted with the development of child psychiatry in this country; this is followed by a description of present trends in pediatric psychiatry and a discussion of opportunities in the future for contributions of pediatrics and psychiatry to each other.

The choice of topics and the arrangement of their presentation in this paper and in one on "Role of Psychiatry in a Childrens Hospital Service," to be published in a later issue, were dictated by the desire to assist in the further coequalization of the function of pediatrics and psychiatry in child study and care and by the wish to pay honor to Dr. Benjamin Knox Rachford, who as scientist, physician, medical educator and citizen broadly and deeply influenced the direction of pediatrics during many of its years of greatest growth and achievement.

HISTORICAL BACKGROUND

The beginning of pediatrics as a medical specialty in the United States is not sharply delineated within a specified time period. Its birth and development must be viewed as one event in medicine which along with other occurrences in science, the arts and letters, general education, politics, sociology and business goes to make up American history. Although the literature of our country contains allusions to diseases and physical hygiene of infancy and childhood from as early a date as 1677, when the Reverend Thomas Thatcher first published his broadside titled: "A Brief Rule to Guide the Common People of New England How To Order Themselves and Theirs in the Small-Pox, or Measles," American physicians did not study disorders of the early periods of life systematically or intensively until about the middle of the nineteenth century. The years 1830 to 1850 formed a new era in the history of science and technology, in which professional scientists devoting their entire time to laboratory and field work replaced part time workers whose place in science was often an avocation rather than a life work. An important by-product of this professionalism was specialization, which was necessitated by the extensive developments in science. The physician, like the farmer, merchant and industrialist,

Benjamin Knox Rachford Lecture, delivered at Children's Hospital, University of Cincinnati, Feb. 5, 1946.

From the New York Hospital, and the Departments of Pediatrics and Psychiatry, Cornell University Medical College.

became aware of the fact that science could help solve his problems and that technology could provide instruments of precision for better diagnosis and more specific therapy.

In this historical setting, medical education changed in the same manner as education in the general and specific sciences. No longer was a professor of geology appointed who in addition taught chemistry and physics; instead, such a teacher was one who as a specialized scientist instructed others only in geology. It was so, too, in medicine. In 1860, at the New York Medical College, Dr. Abraham Jacobi was appointed professor of diseases of children, and in 1861, J. Lewis Smith became clinical professor of diseases of children at Bellevue Hospital, both events presaging the development of pediatrics as a special branch of medicine, without subordination either to obstetrics, as had been the custom heretofore, or to internal medicine, which was simultaneously in the process of evolution. The establishment for the first time of a full time chair of pediatrics in an American medical school occurred in 1888 when Dr. Thomas M. Rotch became professor of pediatrics at Harvard University Medical School, and along with this act, the organization in the same year of the American Pediatric Society and, in 1897, the recommendation of Rachford for the segregation of child patients from adults in hospital pavilions were further indications that the development of pediatrics was part of the natural evolution of medicine in our society, rather than some temporary artefact.

In this setting of vast scientific advancement, the common man in sickness was often either ignorant of the great improvements of medical diagnosis and care or too poor to take advantage of the best practices in medical science, and he continued to use the homemade nostrums which were either carried over in family folklore or advanced by the variety of "new schools of medicine" which began to flourish in the eighteen hundred and thirties and eighteen hundred and forties. The extravagant claims of the pseudohealers who predicted a hygienic millenium through the conscientious use of their dietary panaceas, magical elixirs, syrups, pills, watercures and homeopathic remedies not only confused the people but set up within them a militant spirit of antagonism against orthodox medical practitioners. This resulted in the revocation of state supervision of medical practice in many of the states. The incidence of disease rose, especially among infants and young children, and, although the average citizen opposed public regulations of his own health, he soon saw the beginnings of a public health movement. Individually, physicians like Jacobi, J. L. Smith and Rachford, who were intellectually honest and were leaders who understood the relationship of social and medical problems, interested themselves in the causes of disease which at times reached epidemic

proportions; and through their efforts as practitioners and medical teachers they introduced new methods of infant feeding and preparation of food, especially the boiling of milk. Rachford's contribution through the establishment of The Babies Milk Fund is well known and constituted one of the most important steps in infant care. No wonder the pediatrician became known as the "baby doctor," and pediatrics as a specialty which interested itself in infectious diseases and infant hygiene.

Even though modern psychology was then just beginning, this era in the second and third quarters of the last century saw attempts to use inductive methods in the study of mental life. Supernaturalism and superstition were rife, and out of them developed the cult of animal magnetism and the practice of mesmerism. Although attempts were made to confuse religion, therapy and materialism, there was some experimentation by physicians in inductive investigation. It should be recalled that in 1850, when the fake table rappings of the Fox sisters were exciting the nation, physicians were called on by citizens to investigate the phenomenon by scientific methods, and the hoax was soon demonstrated. Phrenology, which was another charlatanism of the period, was less easily exposed; physicians and lay people (who at one time included such prominent leaders of American thought as Horace Mann, President Quincy of Harvard, Poe, Whitman and Emerson) too readily accepted these doctrines as examples of the new scientific spirit of the times. The tenets of phrenology were received so favorably for two reasons: First, Spurzheim, one of the founders of the cult, had visited America and demonstrated to medical men his technic of dissection of the brain, using his personal charm and insight into human nature quite as much as his technical skill to arouse the admiration of his professional audiences; second, the principles underlying phrenology repudiated the traditional philosophy of the times, which seemed metaphysical and academic, whereas phrenology seemed based on a function of something organic, something tangible and visible—that is, the brain and nervous system. The concept that propensities of behavior resided in the brain, which in its growth affected the size of its covering, the skull, and that to analyze character one had only to study the heads of patients appeared to the physician of that time just as logical as the cause and effect relationship between spoiled milk and enteritis now accepted by the pediatrician. The popularization of phrenology ultimately brought discredit to it, but medical formulations for a long time, in fact until only recently, continued to overemphasize either the power of abstract thought over will or the predominance of body and organs over the feelings and emotions.

THE PERIOD FROM 1900 TO 1920

The urbanization of many areas of the country was a strong deterrent to supernaturalism. The city, with its disease-infected slums, stimulated pediatricians like Jacobi, Smith and Rachford to fight contagious disease with new weapons which had come from the European laboratories of Pasteur, Lister and Koch; and just before the end of the last century these innovations bore gratifying results in the form of a decline of mortality of 10 per cent, largely in the age groups of infancy and childhood, and a rise in life expectancy from thirty-one to thirty-five years. Although the major attention and interest of pediatricians in the first quarter of the twentieth century continued in the fields of pathology, diagnosis and treatment of diseases and malformation and dysfunction of organs, the continuance of investigation in preventive medicine and of practice in public health as corollaries to pediatric practice seemed natural because of the gratifying results which followed earlier endeavors in these fields. In fact, the correlation of pediatrics and public health became so close that in 1914 Hamill, as president of the American Pediatric Society, described preventive medicine as synonymous with public health and admonished the pediatrician to remember that "the maintenance of public health means practically the maintenance of the health of the child." In 1923, also in a presidential address before the same society, L. Emmett Holt predicted the development of a "public health pediatrist," who would take the lead in health teaching. Jacobi [1] as early as 1889 had defined the scope of pediatrics by saying: "Pediatrics deals with the entire organism"; "The connection of pediatrics with neurology is very intimate indeed"; and, further, "Neurology's sister, psychology, is indebted for much of its wealth to the study of the intellectual life of infancy and childhood," and "Psychiatry, too, has learned from the mental aberrations occurring at an early age." This statement turned out to be more than a definition of pediatrics, being also a prediction of the stages through which this discipline of medicine would develop.

In terms of mental health and disease, pediatric attention was first turned toward neurologic problems. This interest in organic pathology, especially of the brain, paralleled a similar interest held by psychologists and stemmed largely from the influences just described in the period of American history when ideas of superstition were abundant. The human mind was regarded, as it had been for centuries, in the belief that all nervous tissue was patterned after a common mold and that the mind, as nervous tissue, existed independently of the rest of the

1. Jacobi, A.: The Relations of Pediatrics to General Medicine, Arch. Pediat. 6:758, 1889.

body. Toward the end of the nineteenth century, which might be characterized as the end of the period of general interest in spiritualistic manifestations, disciples of the German, Wundt, began to use objective technics for the study of the mind and, especially, of sensation, so that as a result of the methods of physics and physiology, psychology was transformed more and more into a natural science. The influence of Darwin in this direction was still greater. By demonstrating similarity between the behavior of infants and that of animals and by correlating emotions with bodily expressions, Darwin showed that investigation of the human mind was part of the study of nature; in presenting this concept he antedated the present day concepts of psychosomatic medicine by over half a century. Consideration of the mind in terms of evolutionary concepts was advanced further about the beginning of the 1900's by such psychologists and educators as G. Stanley Hall, E. L. Thorndike, William James and John Dewey. Their researches extended into the field of animal learning and, later, of child learning and, as a result, basically altered the concepts of child training and education and marked the actual beginning of child psychiatry in this country.

It is natural, then, that the next step in the development of pediatrics should be, as Jacobi predicted, in the direction of psychology. The adoption in this country of tests for the measurement of intelligence and for developmental behavior was under way, although the practical usefulness of these criteria was not realized by educator or pediatrician until the standards of Binet were translated by Terman into American values in 1916 and until the American pediatrician Gesell and his co-workers presented their extensive studies on infant behavior and growth. Child psychiatrists in this country quite naturally used this material in greater degree than pediatricians by applying and improving psychometric testing in the training schools for the mentally retarded. Adolf Meyer, known as the father of American psychiatry, made some of his earliest contributions in this field by writing on mental abnormalities in children for the Society for the Study of Child Nature which the psychologist Hall had founded. Rachford again showed his versatility of interests by publishing his book on "Neurotic Disorders of Children," which was printed in 1905 and which dealt with psychologic factors in the causation of mental illness. A few years later, a new outgrowth of psychology appeared in the studies of John B. Watson, who began in 1917 to study the acts of infants prior to learning, as well as the learning process itself. Watson adapted Pavlov's work on the conditioned reflex to children and showed that they could be conditioned and unconditioned to the fear of animals; from this he formulated the well known theory of behaviorism, which interpreted

human nature in terms of reflexes or inherited responses and of acquired and determined responses to internal bodily stimuli and to external stimuli. These studies influenced pediatrics momentously in that they provided the pediatrician and parent alike with new suggestions as to how to rear children. From the standpoint of the development of child psychiatry as a scientific discipline in this country, a gain probably was made through the knowledge of behaviorism, in that mind and body were no longer considered in a dualistic relationship. However, Watsonian teachings created new problems and new conflicts and resulted in the formulation of ideas of child rearing which are still too strongly felt in pediatric practice today, particularly as they create difficulties in the realms of eating, sleeping and habit training (especially toilet training), which seem to make up the bulk of problems with which the modern parent confronts his pediatrician.

THE PERIOD FROM 1920 TO 1945

In considering further the historical scene of this country, especially as it relates to the development of pediatrics and child psychiatry, one comes now to the period just ended, which began with the First World War and continued into the Second World War, comprising years which have been lived through so recently that they seem part of the present rather than historical landmarks of an epoch. The beginning of this period saw pediatrics advancing scientifically under the leadership of John Howland, who, through the stimulation of students and coworkers and through clinical investigation, made discoveries about diseases and their treatment which advanced pediatrics to the important position it occupies today. Simultaneously with this progress in science came changes in the social, economic and even moral spheres, which after World War I took the form of national prosperity, a decline of reform, admonitions in the press for greater individual spending and aspirations on the part of business and professional men alike to be of public service. In this setting, former President Herbert Hoover in 1921, as head of the Child Hygiene Association, took steps to increase the effectiveness of work done in behalf of children, and in 1923 the American Child Health Association was formed through the efforts of pediatric groups. Concomitantly with free spending came a lack of restraint in behavior, and delinquency which had been recognized before the war now assumed alarming proportions.

The next great step in the development of child psychiatry in this country came as a response to an appeal from citizen groups in social work, sociology, psychology, education, law and medicine for the prevention and control of delinquency and mental disease. As a result, an active mental hygiene movement evolved. With the help of the Commonwealth Fund, the National Committee for Mental Hygiene

(about 1920) formulated plans for work in child welfare and, through the development of child guidance clinics, set up a five year plan with the following objectives:

To develop the psychiatric study of difficult, predelinquent and delinquent children in the schools and juvenile courts and to develop sound methods of treatment on such study.

To develop the work of the visiting teacher, whereby the invaluable early contacts which our school systems make possible with every child may be utilized for the understanding and development of the child.

To provide courses of training along sound lines for those qualified and desiring to work in this field.

To extend by various educational efforts the knowledge and use of these methods.

The child guidance clinics have lived beyond the five year period of experimentation and today assume an active role in the psychiatric treatment of children, in parental guidance and in the training of physicians in psychotherapy.

Up to approximately 1930, psychiatry was not integrated with the rest of medicine, and pediatrics saw in medical psychology nothing that it might incorporate into itself except intelligence testing. Pediatricians were still teaching parents the tenets of behaviorism, although the parents themselves were beginning to question, and even resist, advice about child care which was rigid, artificial, mechanical, unfeeling and fitted more to animal experimentation in the conditioning experiment than to a home and parent-child relationship. Dr. Adolf Meyer, of the Phipps Psychiatric Clinic, had long been interested in mental hygiene and child guidance and early stressed the desirability of preventing emotional difficulties in children. His theory of psychobiology stressed the importance of the patient as a person whose life history must be studied, as well as his mental and physical capacities, in order to understand his problems. For this reason Meyer advised the use of social workers, schools and other agencies to provide information about the patient and to help in his life's adjustment. These practical suggestions have not only become basic principles in child psychiatry today but, through the pioneer work of Kanner as liaison psychiatrist between the Harriet Lane Home for Invalid Children and the Phipps Psychiatric Clinic at Johns Hopkins Hospital, have influenced pediatric practice and education to think of mental health as part of physical health.

The last great forces to bring about change in psychiatry and pediatrics as well as in other realms of scientific thought of the country began to be felt about the end of the first quarter of this century and were made up of sociologic and psychologic influences. In this period national prosperity was at its height, and few foresaw the great depression which was impending. After this catastrophe, there is found

in American pediatric literature a theme of pessimism for the future of this specialty which paralleled the moods of depression which were held by people generally. It was in this setting that John L. Morse [2] questioned the ability of pediatrics to survive and, in 1935, that Veeder [3] in a similar vein spoke about the trend in pediatrics and predicted: ". . . that in a few years the general practitioner will take over a large part of the work that is being done by the specialist in pediatrics as he now exists." The latter author, however, was not long pessimistic about the matter, because in the following year he joined Aldrich [4] in the authorship of papers which outlined the scope of graduate education in pediatrics and included child guidance or mental hygiene and growth and development as requisites in training. Other pediatricians, like Casparis [5] and Davison,[6] encouraged the pediatrician to include mental hygiene as part of his practice; in fact, they advised him that pediatrics and mental hygiene were inseparable disciplines. Brennemann,[7] although author of an article titled "The Menace of Psychiatry," actually advocated the integration of psychology into pediatrics and expressed a hope that in the future there might be psychologic pediatricians, who would lead in such a unification. In 1939, Crothers described the quest of "A Pediatrician in Search of Mental Hygiene." Powers,[8] Brennemann [9] and Aldrich [10] deplored the rigidity and impersonality of infant feeding, pointed out the psychologic implications in the feeding of infants and children and recommended a more humane and psychologic approach in all child care.

Many pediatricians began to take heed of the warnings of these colleagues and looked for help in obtaining professional guidance and training which would permit them to carry out the new tasks in mental hygiene which confronted them. It was entirely natural for some of them to turn to the Commonwealth Fund, which had long demonstrated

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2. Morse, J. L.: The Future of Pediatrics, J. Pediat. **10**:529, 1937.

3. Veeder, B. S.: Trend of Pediatric Education and Practice, Am. J. Dis. Child. **50**:1 (July) 1935.

4. (*a*) Veeder, B. S., and Aldrich, C. A.: Graduate Education in Pediatrics, Am. J. Dis. Child. **52**:665 (Sept.) 1936. (*b*) Aldrich, C. A. and Veeder, B. S.: An Outline of the Pediatrist's Relation to Mental Hygiene, J. Pediat. **9**:323, 1936.

5. Casparis, H. R.: Some of the Preventive Aspects of the Mental Hygiene Problem, J. A. M. A. **106**:2207 (June 27) 1936.

6. Davison, W. C.: Preventive Pediatrics, J. A. M. A. **114**:742 (March 2) 1940.

7. Brennemann, J.: Pediatric Psychology and the Child Guidance Movement, J. Pediat. **2**:1, 1933.

8. Powers, G. F.: Infant Feeding, J. A. M. A. **105**:753 (Sept. 7) 1935.

9. Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1937, vol. 1, chap. 25.

10. Aldrich, C. A.: Ancient Processes in a Scientific Age, Am. J. Dis. Child. **64**:714 (Oct.) 1942.

an interest in medical education and psychiatry. The Commonwealth Fund in 1937 established its first fellowships in pediatric psychiatry, which provided training for a period of two years for accredited pediatricians in order that they might on completion of this experience take up teaching positions in pediatric centers and help other pediatricians get a working knowledge of medical psychology, which they might, in turn, incorporate into the practice of pediatrics within the hospital setting and in the care of the ambulatory patient. Dr. Frederick H. Allen, of the Philadelphia Child Guidance Clinic, took an active part in training pediatricians in this fellowship program, and he has been a great force not only in teaching physicians individually but also in encouraging psychiatry to leave its more or less sequestered position and penetrate the other disciplines of medicine, social work and education. The creation of fellowships for the training of pediatricians in psychiatry has continued, so that today at the New York Hospital there are five trainees who on completion of their experience will begin full time positions in public health work at pediatric centers, in order to teach physicians, nurses and workers in related fields how to include mental hygiene practice in their various professions.

As this country passed through the contrasting experiences of having what seemed like a superabundance of all material things to that of a painful lack of even essential articles, there developed with increasing force a psychologic movement which, like the sociologic influence just described, has been of the profoundest importance in changing psychiatry and pediatrics. This influence was the psychoanalytic movement of Freud, whose theories, with modifications by co-workers and pupils, for a time vied with those of the behaviorists. Although there have been reckless and uncritical popularizations as well as unsympathetic diatribes directed against the freudian concepts, it is apparent that these new developments were part of a general movement against scientific absolutism and determinism, which in other fields was championed by such persons as De Vries in biology, Rutherford in atomic research and Einstein, Millikan and Compton in physics. These scientists emphasized that many of the long-accepted views of the universe were not final laws, that there were many uncertainties in science and that "there was a universe of relationships, as well as of matter and motion," [11] and that it was more important to accept a universe of relationships rather than one of matter and motion alone.

What, specifically, has been the effect of the psychoanalytic movement on psychiatry and pediatrics and on child rearing? Briefly, it has demonstrated the dynamic powers of the unconscious, that symptoms and fantasies as well as inarticulated emotions result from the accumula-

11. Curti, M. E.: The Growth of American Thought, New York, Harper & Brothers, 1943.

tion of energies and internal tensions incident to underlying anxiety and that emotional as well as physical processes in the body are regulated by a sum total of psychochemical forces, which function as they do because of the relationship of one's historical past and one's life experiences. These teachings, because they were revolutionary, set up a bitter struggle both within and without American medicine, but nevertheless, as a result of their application, psychiatry has turned its interest from the classification and study of mental disease, especially the psychoses, to the observation of people, both well and sick, in order to learn what the "dynamic mechanisms" of behavior comprised. Such a study of individuals in psychoanalysis by the method of retrospective research not only supplied new information about psychophysiology, psychopathology and psychotherapy but yielded important data about infancy, childhood, adolescence and parental relationships. Not content, however, with these achievements, the psychoanalytic group [12] has increasingly requested that pediatrics, through its interest in the infant and with its opportunity for long term observation of the child growing in its natural habitat, the family setting in a home, study contemporaneously and longitudinally the life histories of their child patients, thus helping not only to fill the gaps in the knowledge of personality development but testing as well those hypotheses which the psychoanalysts themselves question.

Freud and Meyer, although representing different schools of thought, were in agreement in pointing out that personality is a summation and synthesis of all the forms and aspects of the life of the human being—organic, economic, cultural, sociologic and psychologic. Today, adherents of both the psychoanalytic and psychobiologic concepts emphasize the opportunity of pediatricians to join with psychiatrists, physiologists, anthropologists and sociologists in a program of "prospective" research in child development which, with a study of "retrospective" psychoanalysis, promises to yield information from which basic principles of child rearing, child education and child care in health and in sickness may be evolved. The contemporary research work of Washburn of the Child Research Council in Denver and of Aldrich at the Mayo Clinic bears testimony that modern pediatrics has once again recognized the trend of events and has found its place in the mosaic setting of history. The long term comprehensive studies at these two centers will unquestionably furnish data which will augment and modify the conception of the child and his care. This is all in keeping with the history of American thought through the nineteenth and twentieth centuries and foretells the rise of a broad and comprehensive scientific enterprise in human biology, in which various disciplines will take part. That it is

12. Hartmann, H., and Kris, E.: The Psychoanalytic Study of the Child, New York, International Universities Press, 1945, vol. 1, p. 11.

fundamental for pediatrics to take an active part in this new development was emphasized by the experience of many practitioners in World War II, when, as physicians in induction centers and in veteran rehabilitation clinics alike, they were impressed by the number of individuals who were in need of psychiatric guidance because something had gone wrong in their personality development, beginning in infancy and early childhood. The high incidence of psychiatric casualties of the war which antedated combat experience is a well known fact. Not so well recognized are the causes for this great number of psychiatric disturbances, which seem to confront physicians more today than at any other time in the nation's history. With the experience of World War I and its aftermath of delinquency in mind, it is not difficult for one to predict that the country is about to witness a similar result of World War II. Already there is a rise in delinquency, and the numbers of broken homes and the amount of marital discord appear more abundant than they were in the period of the first World War.

A critical review of the methods of child rearing, education and physical and emotional care seems indicated as a first step in an attempt to understand these problems. Where a careful examination has been made, there is evidence that there must be a reorientation of attitudes of child development, parental guidance and medical care, since, in tracing the origin of emotional disturbances, there are repeatedly encountered stories of tension between parent and child as it passes through the various stages of growth, especially tension around the everyday situations of weaning, feeding, toilet and habit training, sleeping and disciplining. The pediatrician again appears at the crossroads in considering how to modify his technics, so that he may serve better the individual parent and child and thereby prevent some of the deviations of personality development which are seen so frequently in all medical practice today. And, as a corollary, educators of pediatricians must consider what changes are in order, to provide them with new insights and abilities to carry on these new functions. Pediatricians who are in training, in practice or just returned from war service are in agreement in requesting—even demanding—opportunities for training in medical psychology of a short term or long term variety. One of the most acute problems in medicine today exists in providing instruction in this field which will be sound and practical and which may be incorporated in a natural fashion into pediatric care. The most promising prospect for such correlative teaching so far has been the long term variety in the pediatric departments of medical schools and of teaching hospitals which have the facilities to study infants, children and adolescents for fairly long periods, both as sick and as convalescent inpatients and as outpatients, and where there are enough well trained teachers representing both pediatrics and psychiatry who are capable

and desirous of relating one discipline to the other. Where the outpatient service includes a carefully supervised well baby clinic and has association with accredited nursery, primary and secondary schools in the community, greater opportunities are provided for the demonstration of physical and mental growth of children.

Such a program of training has been tried out in a few hospitals in this country, one being the New York Hospital and Cornell University Medical College. Participants in this venture have been either two year fellows in pediatric psychiatry whose program in training has been tailored to meet their individual needs or house staff members who, as interns and residents, spent periods varying from nine months to three years in hospital training and were exposed to mental hygiene influences in their contacts with fellows and teachers. Segments of the program are presented to medical undergraduates in lectures and seminars and in clinic experiences, as they progress through the pediatric department from the second to the fourth years of their medical school experience.

It is recognized that such a program of training is permitted to relatively few of the many physicians who want this kind of experience today. It is long in duration, and many physicians whose training in the past did not emphasize the psychologic factors in growth and development are unable now either to become fellows or to undertake further resident training. It is natural, then, that these practitioners should look for short term instruction. It must be recognized, however, that abbreviation may lead to superficiality and oversimplification and either to dangerous carelessness in the use of new insights or to emotional blocking because of feelings of inadequacy. This does not mean that no attempts should be made to formulate study groups for practitioners. At the New York Hospital this is being done through weekly seminar groups, in which six to eight physicians meet for informal discussion of pediatric case material presented by the students after thoughtful preparation. Guidance and general planning of the group study is the responsibility of a senior staff pediatrician who has had training experience for this leadership and who is assisted by social workers and teachers, especially nursery school teachers and others in the community who are able to contribute knowledge of their special skills. Efforts are also made to provide these students with experiences outside the hospital setting, in order that they may learn about children through personal and direct observation.

Although the form and duration of a teaching program in pediatric psychiatry will vary as experimentation in instruction proceeds and as modern pediatrics assimilates new concepts, the content of each program must embrace certain fundamentals.

The following basal topics should be considered:

1. The mental (emotional, social and intellectual) growth and behavior of infants from birth to maturity, with consideration of the interplay of hereditary, somatic, psychologic, interpersonal and cultural forces which takes place in the development of each person from conception onward.

2. The psychologic implications of child bearing and rearing, education, and child care in health and in sickness, especially in terms of parent-child relationship but including other interpersonal relationships involving the parent and child.

3. The psychologic concomitants of physical illness and the psychologic role of the physician and nurse in parental guidance and in medical treatment of sick children and adolescents.

4. Deviant personality structure and psychopathology, especially in psychosomatic relationships, with emphasis on the genesis, prevention and treatment of emotional difficulties and so-called behavior problems of all age groups from birth through adolescence.

5. Opportunities for psychotherapy in pediatric practice as well as knowledge of the limitations of such endeavors, with attention to the means of preparing patients for treatment by psychiatrists.

It is desired that the pediatrician trained in this manner will become more than just a therapeutic instrument. Instead, by combining new skills of medical psychology with his old abilities of patient care, he should become part of the synthesis of many disciplines, both within and without medicine, which will lead to a broad and comprehensive scientific enterprise called "human biology," which it is hoped will contribute to the advancement of social progress in this country.

Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

BACTERICIDAL ACTION OF ANTIBIOTIC SUBSTANCES. SELMAN A. WAKSMAN and H. CHRISTINE REILLY, J. Infect. Dis. **75**:150 (Sept.-Oct.) 1944.

A comparative study of the antibacterial action of various antibiotic substances on different bacteria, representing both gram-positive and gram-negative forms, permits the following conclusions:

Antibiotic substances not only are bacteriostatic but possess distinct bactericidal properties.

Those antibiotic substances that are characterized by a high bacteriostatic activity against certain bacteria also exert a marked bactericidal action against the same organisms.

Some antibiotic substances fail to inhibit the growth of all the bacterial cells in a given population or culture. This leads to the gradual adaptation of a few of the surviving cells to the antibiotic agent. Other substances, however, are characterized by the complete destruction of all the bacterial cells in a given population; the concentration of the substance is of importance in this connection.

The differences in the bactericidal action of antibiotic substances on various bacteria point to differences in the mode of action of these substances and in the specific sensitivity of the bacteria toward them.

The bacteriostatic versus the bactericidal action of antibiotic substances throws light on the specific "biochemical makeup" of each bacterial species. This phenomenon transcends that of differences in the staining reaction or in the nutritional requirements of the specific bacteria. It is illustrated by two apparently uncoordinated facts: 1. Penicillin does not act on most of the gram-negative organisms but acts readily on most of the gram-positive forms, whereas streptotrichin acts on many bacteria within each of these groups. 2. Both these substances fail to act readily on the mycoid bacilli, whereas streptomycin, a substance in many respects similar to streptotrichin, acts readily on these organisms. Ability to take the Gram stain is only one of the properties of specific bacteria, and not at all an absolute one, that point to differences in the effect of antibiotic substances on the bacterial cell. Other biochemical characteristics of the organisms that are not as yet recognized appear to be highly significant in this connection.

With the use of the dilution and the diffusion methods for measuring the activity of antibiotic substances against several bacteria, it is possible to demonstrate that their mode of action is complex and is controlled by the specific bacterium acted on or used as a test organism.

TOOMEY, Cleveland.

A COMPARISON OF VARIOUS METHODS OF DEMONSTRATING INFLUENZA VIRUS IN THROAT WASHINGS. M. D. ETON, M. COREY, W. VAN HERICK and G. MEIKLEJOHN, Proc. Soc. Exper. Biol. & Med. **58**:6 (Jan.) 1945.

Throat washings, 83 in number, obtained from military personnel in the epidemic of influenza A in 1943-1944 were inoculated into ferrets, hamsters and chick embryos. The diagnosis of influenza in most cases was also established by the complement fixation and chicken cell agglutination tests on human serums.

The results of inoculation of the throat washings from 62 patients into ferrets are summarized as follows: None of the throat washings from 23 patients with

negative serologic reactions for influenza A produced any response in antibodies to influenza virus A, and 17 of the throat washings from 30 patients with positive serologic reactions for influenza A produced an increase in antibodies to influenza virus A in the ferrets (with 2 exceptions, all the ferrets showing an increase in antibodies gave a febrile reaction two to three days after inoculation). None of the ferrets showed an increase in antibodies to influenza virus B.

Each of 55 throat washings was inoculated into 2 hamsters. Of the 20 throat washings which produced a positive response in ferrets, 17 also produced a positive reaction in hamsters; 30 of the 53 specimens from patients known to have influenza A produced a positive reaction in hamsters (as they did in ferrets); 12 throat washings that produced no reaction in ferrets also produced no antibody response in hamsters.

The results of chick embryo studies were as follows: Of the 17 throat washings which had given positive reactions in the ferret and hamster studies, 7 infected chick embryos by the amniotic route (4 on the first passage and 3 on the second), and virus was demonstrated in 2 of 13 unfiltered throat washings in the first allantoic passage. (Zephiran chloride in 1:20,000 dilution did not effectively remove bacteria.)

The studies of the authors indicate that hamsters and ferrets are equally reliable as experimental animals in demonstrating influenza virus A in throat washings, whereas chick embryos are less reliable but amniotic inoculation has the adyantage of requiring three to ten days for identification of the virus, as compared with ten to fourteen days with ferret and hamster inoculation.

HANSEN, Galveston, Texas.

Metabolism; Infant Feeding; Milk and Other Foods

STUDIES ON THE COMPARATIVE NUTRITIVE VALUE OF FATS. HARRY J. DEUEL JR., LOIS F. HALLMAN and ELI MOVITT, J. Nutrition **29**:309 (May) 1945.

The authors conclude that a vegetable fat such as that contained in a margarine (fortified with vitamin A) can serve adequately in place of butterfat for growth and reproduction on a diet otherwise nutritionally satisfactory.

FREDEEN, Kansas City, Mo.

THE NUTRITIVE VALUE OF THE FATTY ACIDS OF BUTTER INCLUDING THEIR EFFECT ON THE UTILIZATION OF CAROTENE. ELIZABETH F. BROWN and WALTER R. BLOOR, J. Nutrition **29**:349 (May) 1945.

The authors observed that when the fatty acids of butter were obtained in five fractions, designated as volatile, low molecular weight liquid, high molecular weight liquid, low molecular weight solid and high molecular weight solid and substituted for the milk fat in a normal diet the efficiency of the butter diet in producing gains in body weight was either matched or improved on by the liquid acid diets. Much of the difference in efficiency between the liquid and the solid acid diets can be explained by the poorer absorption of the solid acids. It was also noted that the rats receiving the unsaturated acids had an improved utilization of the carotene from carrot.

FREDEEN, Kansas City, Mo.

THE AVAILABILITY OF SOYBEAN OIL MEAL PHOSPHORUS FOR THE RAT. ROBERT R. SPITZER and PAUL H. PHILLIPS, J. Nutrition **30**:117 (Aug.) 1945.

The authors found that the phosphorus of soybean oil meal was readily available for growth and bone formation.

FREDEEN, Kansas City, Mo.

Vitamins; Avitaminoses

THE EFFECT OF THE LEVEL OF PROTEIN IN THE DIET ON THE UTILIZATION OF VITAMIN A. MARIE DYE, IONE BATEMAN and THELMA PORTER, J. Nutrition **29**:341 (May) 1945.

The relation of the level of protein in the diet to the utilization of vitamin A was studied on 288 rats by Marie Dye, Ione Bateman and Thelma Porter. They concluded that the level of protein had very little effect on the utilization of vitamin A, as judged by gains in weight, length of the rat and incidence of foci of keratinized epithelium. The level of vitamin A intake was directly related to the rate of gain up to the level of 3 U. S. P. units per day regardless of the level of protein in the diet. On low vitamin A intakes an increase in polymorphonuclear cells was noted.

FREDEEN, Kansas City, Mo.

THE AVAILABILITY OF VITAMINS FROM YEASTS. HELEN T. PARSONS, ANNE WILLIAMSON and MARY L. JOHNSON, J. Nutrition **29**:373 (June) 1945.

The authors found that two types of bakers' compressed yeast, fed fresh to human subjects, were poorly utilized as sources of thiamine, as indicated by low urinary and high fecal elimination of thiamine. These yeasts appeared even to have decreased the amount of available thiamine supplied by the basal diets.

FREDEEN, Kansas City, Mo.

PHYSIOLOGIC AVAILABILITY OF THE VITAMINS. DANIEL MELNICK, MELVIN HOCHBERG and BERNARD L. OSER, J. Nutrition **30**:81 (Aug.) 1945.

Melnick and his co-workers have found that in vitro tests indicate that various fish products intended for direct human consumption contain a thiaminase which destroys thiamine in a static test system. Rapid and complete destruction of the vitamin occurred in vitro during incubation of food mixtures containing added thiaminase, as present in raw clams.

FREDEEN, Kansas City, Mo.

STUDIES ON THE PROLONGED MAINTENANCE OF ADULT DOGS ON PURIFIED DIETS. A. O. SEELER and R. H. SILBER, J. Nutrition **30**:111 (Aug.) 1945.

The authors observed that the dietary requirement of pantothenic acid for the adult dog was so small that the production of pantothenic acid deficiency was a slow process. This decrease in dietary vitamin requirements may be due to an actual lowering of the metabolic requirements for the vitamins, an increased intestinal synthesis or a combination of both.

FREDEEN, Kansas City, Mo.

Hygiene; Growth and Nutrition; Public Health

STUDIES OF THE CENTER OF GRAVITY IN THE HUMAN BODY. CARROLL E. PALMER, Child Development **15**:99 (June-Sept.) 1944.

A method and apparatus for determining two planes, the transverse and the frontal, which pass through the center of gravity of the living human body are described. The technic was applied to the study of 1,200 subjects, whose ages ranged from 6 fetal months to 20 years. In addition to determination of the two planes of gravity, the sex, age, weight, body length, stature, sitting height, pubic height, arm length and leg length were observed for each subject.

The distance of the center of gravity above the soles, expressed as an index or percentage of stature, is represented by a fairly constant figure, which ranges from 55 to 59 during the whole of the developmental period. The most precise statement of the relationship between the stature and the distance of the center of gravity from the soles is the equation $y = 0.557\ X + 1.4$ cm., where y equals the

distance of the center from the soles and X equals stature. Variation about this regression line is low.

Changes in the anatomic position of the center of gravity are shown by a series of midsagittal figures, on which the probable area of the centers is drawn. The descent of the center from the level of the seventh dorsal vertebra to the level of the first sacral vertebra is illustrated and described.

EXTENSION OF HYGIENE AND MEDICAL ASSISTANCE TO THE RURAL CHILD. PEDRO DANIEL MARTÍNEZ, Bol. Inst. internac. am. de protec. a la infancia **18**:430 (Sept.) 1944.

The author, general chief of hygiene and child welfare in Mexico, begins his article by stating that the state in which the rural child lives is deplorable—almost naked, silent, taciturn and hungry—and says that this state of neglect has been going on for centuries. Those children and adolescents who live in the country, in miserable huts and in little villages, number about 5,000,000; only 3,000,000 live in cities and towns of 2,000 inhabitants. Infant mortality is very high; nearly 500,000 children are born every year in rural areas, and of these 100,000 die before they are 1 year old.

Even though there is much to be done, medical assistance to the rural child is now being stimulated, and a group of 1,000 doctors are giving themselves up to work in behalf of the rural child; last year 200,000 inhabitants were vaccinated against smallpox and 230,000 against typhoid, and 178,000 patients were examined.

At present there are 250 centers of hygiene; outside the federal district there are 1,313 centers especially established to assist mothers and children; in these maternity and hygiene centers 250,000 children and 80,000 mothers received assistance, with a total of 500,000 clinical consultations. In the maternity centers of the different provinces 15,000 childbirths took place, and in private homes, 1,800, all of which were attended to.

To struggle against malnutrition, Drs. Gustavo Baz, Manuel Garino and José Pagola, among other measures, are encouraging the cultivation of the soy bean. Moreover, a book on general hygiene is being prepared, with the purpose of spreading its principles through the rural school.

The author ends his article remembering what the president of the Republic once said in a message: "Doctors and teachers form a united army which cooperates in a campaign of progress and emancipation," and he concludes by saying: "And, I add, the education and instructions in hygiene which we give to the rural community will be their best weapons in defending the political freedom and economic prosperity for which they have struggled; for their culture and hygiene they should also struggle, for health and liberty are not natural gifts but are to be won by conquest. And so it is that the hygiene of the country will be the work of the countryman himself; the government, the teacher and the school master should provide him only with the weapons to fight for it."

AUTHOR'S SUMMARY.

PROBLEM OF CRIPPLED CHILDREN OF SCHOOL AGE, MONTEVIDEO, URUGUAY. JUAN E. CENDÁN ALFONZO, Bol. Inst. internac. am. de protec. a la infancia **18**:662 (Dec.) 1944.

Crippled children attending school do not present a medical pedagogic problem except in a few cases, which are mentioned. The physical defect has no effect on the average attendance at school of crippled children as compared with normal children.

The progress attained by the crippled children is equal to that attained by the normal ones. The physical defect has no appreciable effect on the mental development of the child.

AUTHOR'S SUMMARY.

SCHOOL LUNCH ROOMS IN MONTEVIDEO, URUGUAY: THEIR FUNCTION, RESULTS AND MEDICOSOCIAL EFFECT. EUGENIA S. YANNUZZI, Bol. Inst. internac. am. de protec. a la infancia **18**:674 (Dec.) 1944.

Among Uruguayan school children the most common cause of malnutrition is deficiency of food due to lack of economic resources. The lack of economic resources results partly from unemployment, partly from ignorance and especially from alcoholism, which should be effectively attacked.

It is necessary to improve the economic status of Uruguayan families. It is also necessary to teach the population the requirements of nutrition as well as the best economic way to meet them.

Malnutrition should be considered a social evil; protection should be given to the undernourished school child not as charity but as a social duty, as the granting of a right based on the principles of human solidarity.

Establishment of lunch rooms for mothers would be a help in bringing about the solution of the problem of child feeding, for if the mother is well fed during pregnancy many of the future problems will be avoided.

Special attention should be given to protection of the preschool child, for many deficiencies of the school child are due to lack of attention during that period of the child's life. Therefore more lunch rooms should be established for preschool children, so that they may have well balanced, adequate and sufficient food.

EDITOR'S SUMMARY.

Newborn

MEDICAL PROGRESS: DISEASES OF THE NEWBORN. STEWART H. CLIFFORD, New England J. Med. **232**:42 (Jan. 11) 1945.

The infant mortality during the first year of life for the United States in 1941 was 45.3 deaths per 1,000 live births. Of the deaths 61 per cent took place in the first month of life, while 29 per cent occurred in the first twenty-four hours of life.

Prematurity.—Many small premature infants have survived in an atmosphere containing 50 per cent oxygen for several months or until they have developed sufficiently to live under normal atmospheric conditions. Stevenson has made an important clinical application of the use of carbonic anhydrase in disease of the newborn. The action of this biologic catalyst is to expedite the liberation of carbon dioxide from carbonic acid. The infants have the power to metabolize carbohydrate as efficiently as do full term infants. Levine and Gordon are convinced that the failure of some premature infants to thrive on presumably adequate diets may be the result of faulty absorption of ingested fat. Their feeding mixture contains 120 calories per kilogram of body weight, and the total fluid volume is 150 cc. per kilogram, the basic constituents being 2.5 Gm. of fat, 18 Gm. of carbohydrate and 6 Gm. of protein per kilogram. When fluid intake was below 95 cc. per kilogram, large amounts of water were withdrawn from the body and this resulted in a negative water balance and dehydration. The authors recommend that all premature infants be given 25 to 50 mg. of ascorbic acid daily from birth and from 75 to 100 mg. daily after feedings of cow's milk have been instituted. A reduced prenatal storage of calcium, of phosphorus and possibly of vitamin D predisposes the premature infant to rickets.

Miscellaneous Congenital Defects.—Gregg reported on a series of 78 patients with congenital cataract, 44 of whom also had congenital heart disease, the condition occurring in infants whose mothers, with few exceptions, had suffered from what was presumed to be German measles in the early months of pregnancy.

Esophageal Atresia and Tracheoesophageal Fistulas.—Esophageal atresia and tracheoesophageal fistulas were formerly considered incompatible with life. Ladd has recently reported on 39 patients with such defects operated on at the Children's Hospital, of whom 11 are living.

Spina Bifida and Cranium Bifidum.—Ingraham and Swan have analyzed these conditions in 546 infants and children seen at the Children's Hospital during the last twenty years to see whether there can be established any reasonably definite criteria for prognosis, for operative therapy and for operative technics. The authors found that 30 per cent of the patients with spina bifida and 34 per cent of those with encephalocele may expect a relatively normal life.

Congenital Cerebral Palsy.—Yannet analyzed the cases of 86 patients for whom the diagnosis of congenital cerebral palsy had been made and uncovered data showing the major importance of developmental cerebral defects in the causation of the palsy as well as information on certain genetic relations.

Erythroblastosis Fetalis.—This intrauterine hemolytic disease of the fetus and the newborn infant occurs under highly specific conditions, determined by the presence or absence of the Rh factor in the parents. In more than 90 per cent of the cases, the father's blood contains the Rh factor (Rh positive), the mother's blood lacks the factor (Rh negative) and the fetal blood possesses it (Rh positive). Diamond has been able to pool and concentrate low titer anti-Rh serums, obtaining a globulin fraction that yields accurate typing results. Potter insists that to diagnose erythroblastosis anemia, erythroblastemia and splenomegaly must be present. Other manifestations usually associated are edema, jaundice, hepatomegaly and placental hypertrophy. The treatment of erythroblastosis fetalis is by transfusion of Rh-negative blood from a donor other than the mother.

Infection.—In a number of hospitals in different localities epidemics of diarrhea among newborn infants have been associated with mortality rates of from 30 to 50 per cent. The plan of treatment at both the Boston Lying-in Hospital and the Children's Hospital calls for an immediate threefold system of isolation: physical isolation of infected patients; physical isolation of all contacts, and physical isolation of all newly admitted patients from contact with either of the two preceding groups. Active treatment of infected patients is based on the suggestions of Twyman and Horton, which are as follows: succinylsulfathiazole 1 grain (0.06 Gm.) per pound (453 Gm.) of body weight per day, opiates by mouth, vitamin K, transfusions of plasma or whole blood, fluids parenterally and protein milk formulas. In addition to these procedures, the infants are given from 12,000 to 24,000 units of penicillin per day in divided doses every three hours.

GENGENBACH, Denver.

Acute Contagious Diseases

THE EPIDEMIOLOGY OF ACUTE RESPIRATORY INFECTIONS CONDITIONED BY SULFONAMIDES: III. EFFECTS OF TREATMENT ON THE ORGANISM AND CARRIER OF DIPHTHERIA. L. A. JULIANELLE and MORRIS SIEGEL, Ann. Int. Med. **22**:21 (Jan.) 1945.

Continuous administration of sulfadiazine did not prevent either the dissemination of Corynebacterium diphtheriae among exposed children or its repeated recovery on culture of materials from the throats.

Under the conditions outlined in the article, sulfadiazine did not inactivate preformed toxin or prevent the elaboration of toxin.

The drug was ineffective as a method of treatment.

READING, Galveston, Texas.

LACK OF SALT MAY BE CAUSE OF POLIOMYELITIS. JAMES F. RINEHART, California & West. Med. **61**:268 (Nov.) 1944.

Lack of sufficient salt in the body may be one of the factors that predispose a child to poliomyelitis. That epidemics of poliomyelitis always come in the summer months, when copious perspiration removes salt from the system, and that active,

robust children are more likely to be stricken suggest that salt depletion may be one of the causes of susceptibility to this disease. Likewise, the disease seems to attack children who recently have been physically overactive.

Studies of 30 patients during a recent epidemic revealed that the chloride concentrations of whole blood were generally lowered and the spinal fluid concentrations were moderately lowered. The cell volumes were increased, which might indicate that the depletion of salt in the serum caused a flow into the blood cells.

Further clinical studies, as well as animal investigations, are recommended. The author suggests that in the meantime children should be given plenty of salt in the summer months to make up for the large amounts excreted in perspiration.

PRYOR, Palo Alto, Calif.

VENTILATION IN THE SPREAD OF CHICKENPOX AND MEASLES WITHIN SCHOOL ROOMS. MILDRED WEEKS WELLS, J. A. M. A. **129**:197 (Sept. 15) 1945.

The school ventilation standard of 30 cubic feet (0.9 cubic meter) of air per minute per child is both difficult to attain and inadequate to prevent classroom spread of chickenpox and measles except in relatively immune classes (less than 40 per cent susceptible to chickenpox, less than 20 per cent susceptible to measles).

Radiant disinfection of air can be substituted for actual replacement of air. In the experiments reported here, the ultraviolet radiation increased, in all susceptibility groups and in case of the three diseases tested—chickenpox, measles and mumps—the chance that an exposure would be negative.

AUTHOR'S SUMMARY.

THE PSYCHIATRIC SEQUELAE OF POST-MEASLES ENCEPHALITIS. E. C. SMITH and CARL E. TRAPP, J. Nerv. & Ment. Dis. **100**:555 (Dec.) 1944.

In this study of 21 cases the author reviews the history of the patients prior to the development of measles encephalitis, the neurologic changes associated with the disease and the social and intellectual adjustment of the patients for more than five and one-half years after recovery. Five cases are described in detail.

JAHR, Omaha.

RESULTS IN THE TREATMENT OF MENINGOCOCCIC MENINGITIS WITH ANTITOXIN AND SULFONAMIDE DRUGS. JOHN H. DAVIS, WILLIAM J. MORROW and JOHN A. TOOMEY, J. Pediat. **26**:455 (May) 1945.

In the Department of Contagious Diseases, City Hospital, Cleveland, an overall mortality rate of 13.2 per cent was obtained for 309 patients ill with meningococcic meningitis and treated with a combination of sulfonamide drugs and antitoxin. The mortality rate was only 8.8 per cent when those patients who were dead on arrival or who were moribund and died within forty-eight hours were excluded. This mortality rate of 8.8 per cent would be even lower—i. e., 7.6 per cent—if those patients who died from other conditions (although these conditions were initiated by the meningitis) were omitted.

In general practice, physicians should strive for the same low mortality rate as that obtained in military medical practice, but it must be remembered that the civilian patient may be of any age and may have an underlying pathologic condition which makes recovery almost impossible.

TOOMEY, Cleveland.

THE WATERHOUSE-FRIDERICHSEN SYNDROME. VINCENT C. D'AGATI and BRUNO A. MARANGONI, New England J. Med. **232**:1 (Jan. 4) 1945.

A report is made of 6 cases of the Waterhouse-Friderichsen syndrome. A case of recovery is discussed in detail, and the literature on recovery of patients with

this syndrome is reviewed. The significance of the renal failure as evidenced by the initial anuria followed by oliguria has heretofore not been fully appreciated. The roles of bacteremia and shock in the pathogenesis have been overemphasized. Death in all cases is probably the effect of the overwhelming toxemia, which in the short-lived patients results in profound shock and in those with relatively long survival periods leads to hepatorenal failure. The reestablishment of renal function heralded recovery and was the most important prognostic sign. The authors believe that the meningococcus is the sole etiologic agent in the Waterhouse-Friderichsen syndrome.

The intravenous administration of 500 cc. of plasma, repeated in twelve hours, is recommended because of its osmotic effect, mirrored in a noticeable elevation of the blood pressure. The use of epinephrine is of questionable value. It seems advisable to administer antimeningococcus serum in adequate amounts—60,000 to 120,000 units—intravenously within the first twenty-four hours. The initial dose of sulfadiazine in this series, all young adults, was 5 Gm. intravenously and 18 Gm. orally. This was followed by large oral doses until a total of 25 to 30 Gm. had been given within the first twenty-four hours. The blood concentration of sulfadiazine was used as a guide for determining the size and frequency of subsequent doses. The optimal blood level was considered to be 15 to 20 mg. per hundred cubic centimeters.

GENGENBACH, Denver.

POLIOMYELITIS VIRUS IN THE BLOOD STREAM IN THE EXPERIMENTAL DISEASE. J. L. MELNICK, Proc. Soc. Exper. Biol. & Med. **58**:14 (Jan.) 1945.

Of all the attempts made to isolate poliomyelitis virus from the blood of human subjects, none has been successful except one (Ward, R.; Melnick, J. L., and Horstmann, D. M.: *Science* **101**:491, 1945). Three strains of poliomyelitis virus originating in human stools of patients from Texas (1942), Hartford, Conn. (1942) and various sections of the country (1940-1941) were injected into rhesus and capuchin monkeys. Blood was collected from the heart and prepared by ultracentrifugation, then inoculated intracerebrally into a rhesus monkey. The criterion for a positive reaction (i. e., demonstration of a virus in the blood, the contents of the colon or the spinal cord) was the production in the test animals of typical histologic lesions, viz., neuronophagia and neuronal necrosis associated with perivascular and interstitial cellular infiltration. Virus was found in the blood stream of 4 of 7 monkeys infected with the Hartford strain and in none of the 3 monkeys infected with the other strains. Of the 10 monkeys which were paralyzed after being inoculated with virus of human origin, 3 rhesus and 1 capuchin monkey were found to have virus in the blood stream. In only 1 of the animals was the virus found in the colon contents.

HANSEN, Galveston, Texas.

Acute Infectious Diseases

SUPPLEMENTAL USE OF ERGOTAMINE IN ELICITING TRANSIENT DISTURBANCES OF RHYTHM IN ACUTE RHEUMATIC FEVER. MARTIN H. WENDKOS, Proc. Soc. Exper. Biol. & Med. **58**:303 (April) 1945.

Ergotamine tartrate, 0.5 mg., was injected intravenoulsy into 8 soldiers with polyarthritis, in most of whom there was no clinical evidence of cardiac disease, and electrocardiographic tracings were made before and thirty to sixty minutes after injection. On 5 of the patients similar studies were made after evidence of activity of the rheumatic infection had disappeared. In 6 patients distinct disturbances in rhythm developed after the medication: First degree auriculoventricular block was found in 4 patients, a second degree auriculoventricular block with dropped beats in 1 patient and nodal rhythm with a first degree block in another. In the 5 patients who were tested later the response was the same as

that noted in normal persons, namely, a slight slowing in the sinus rate. It is considered that the rationale of this procedure depends on the elevation of a subordinated or "latent" hypervagotonia by a suppression of activity of the normal antagonist of the vagus nerve, so that "cholinergenic" disturbances in rhythm are thus made manifest in the electrocardiogram.

HANSEN, Galveston, Texas.

Chronic Infectious Diseases

THE TREATMENT OF SEVERE TUBERCULIN REACTIONS. J. D. PILCHER, Am. Rev. Tuberc. **49**:556 (June) 1944.

Occasionally the intracutaneous injection of tuberculin leads to a severe local reaction which may result in vesiculation, sloughing of tissue and scar formation. To combat this, Pilcher has found the continuous application of cold in the form of an ice bag is effective. It is necessary that the application be continuous and that the ice bag remain in place until the reaction subsides, which may be for a period of several days. Should a reaction give evidence of becoming severe, this procedure properly applied causes it to remain stationary or allows it to progress but slightly.

EUGENE SMITH, Ogden, Utah.

BOVINE TUBERCULOSIS IN THE UNITED STATES: ITS CONQUEST AND EFFECT ON PUBLIC HEALTH. H. R. SMITH, Am. Rev. Tuberc. **50**:520 (Dec.) 1944.

This interesting paper by a layman, the general manager of the National Livestock Loss Prevention Board, is a historical review of the steps leading up to the control of bovine tuberculosis. The success of this enterprise has been due to the combined efforts of meat packers, producers and local state and federal agencies. That these efforts have been successful is evident from the fact that in 1916 of all cattle slaughtered under Federal inspection in the United States 2.35 per cent were retained because of tuberculosis, while in 1943 the per cent was 0.048. In the same year the incidence of the disease in all cattle had been reduced 98 per cent.

It has not as yet been possible to control tuberculosis in hogs to so great an extent. These animals become infected from the droppings of chickens, and avian tuberculosis is the prevailing type found. Avian tuberculosis is not commonly transmitted to human beings; hence the problem is not so serious as that of bovine tuberculosis. Nevertheless, in 1943, 7 per cent of all hogs slaughtered under Federal inspection were retained for this disease and a considerable number were destroyed.

The effect this program has had on human tuberculosis can only be conjectured. The mortality figures, however, are very suggestive. In 1917, when the program for the control of bovine tuberculosis was initiated, the human death rate for respiratory tuberculosis in the United States was 124.6 per hundred thousand of the population and 22.5 for other forms. In 1942 the rates were 39.6 and 3.5 respectively.

EUGENE SMITH, Ogden, Utah.

THE PROBLEM OF TUBERCULOSIS CONTROL. J. A. FOLEY and J. B. ANDOSCA, New England J. Med. **231**:86 (July 20) 1944.

In summary the authors state that even if it is not possible at present to eradicate pulmonary tuberculosis, owing to its multiple and complex aspects, at least a well managed and efficient program of tuberculosis control can and should be employed. This will surely bring about a definite reduction in the economic burden, the mortality and the morbidity rate resulting from pulmonary tuberculosis.

GENGENBACH, Denver.

BONE LESIONS OF CONGENITAL SYPHILIS IN INFANTS AND ADOLESCENTS: REPORT OF 46 CASES. P. E. RUSSO, and L. F. SHRYOCK, Radiology **44**:477 (May) 1945.

Roentgenologic observations in 46 cases of congenital syphilis are evaluated in a table, which indicates the frequencies of various osseous lesions as follows: periostitis (42), osteochondritis (21), osteitis (17), osteomyelitis (11) and fractures (5). Of children over 1 year of age the roentgenologic changes caused by periostitis and osteochondritis in only 1 showed. The frequency of osteitis and periostitis dropped 50 per cent.

Osteochondritis is described as a zigzag or "saw-tooth" appearance of the metaphysis. This is considered pathognomonic in children under 1 year of age. A sclerotic zone or cap is seen if utilization of calcium becomes unbalanced.

Periostitis varies from a thin to a thick linear shadow which parallels the cortex. It may be the only roentgenologic sign.

Osteomyelitis may occur as a single lesion or in a more generalized form, as in the pyogenic type.

Osteitis is found almost exclusively in the older children and is most commonly bilateral. The cortical bone is thickened and of increased density. Under adequate management for syphilis, healing occurs rapidly.

In the majority of cases a combination of the previously described lesions are found.

Serologic reactions were positive in 43 and negative in 2 of the 46 cases. Illustrations of osseous changes in 6 cases are included in the report.

AMSPACH, Chicago.

OBJECTIVES AND RADIOLOGICAL ASPECTS OF TUBERCULOSIS CONTROL PROGRAM. HERMAN E. HILLEBOE and RUSSELL H. MORGAN, Radiology **45**:185 (Aug.) 1945.

An effective program for control of tuberculosis, embracing four principal phases, is described. These are as follows:

1. *Case Finding.*—Of first consideration are groups of the population in which a high prevalence is suspected and in which large numbers of persons can be reached quickly and economically. Familial epidemiologic studies which have been found inadequate should be supplemented by mass roentgenography (use of miniature films), which has been only recently introduced. This procedure is probably necessary for a limited number of the population, namely, persons admitted to general hospitals and industrial employees. Routine roentgenograms of the chest are recommended for these groups. The United States Public Health Service, authorized by the Seventy-Eighth Congress, plans to furnish financial assistance for mass roentgenography to state, city and other health groups.

2. *Medical Care and Isolation.*—Institutional care should be supplemented by well located clinics for thoracic diseases, generous public health nursing, accessible laboratory services and active participation of family physicians.

3. *After-Care and Rehabilitation.*—Patients must make satisfactory readjustment to a way of living after returning home. Proper guidance during their stay in the hospital will prepare the way for effective rehabilitation. Services of social workers, educational psychologists and employment officers are often essential in outlining work most suitable for the patient. Part time or modified employment may be necessary.

4. *Protection of the Tuberculous Family Against Economic Distress.*—To avoid economic distress to the patients' families and to allow for full hospitalization of the patients, a national plan to provide against loss of wages during treatment and for several years after arrest of the disease is the only logical answer to this problem.

AMSPACH, Chicago.

Diseases of Blood, Heart and Blood Vessels and Spleen

A Study of Hemoglobin Formation Following the Administration of Certain Amino Acids to Rats Fed a Diet Low in Protein. Aline Underhill Orten and James M. Orten, J. Nutrition **30**:137 (Aug.) 1945.

It was observed by the authors that no consistent, sustained increase in hemoglobin values occurred following supplementation with any of the ten "essential" amino acids or with aminoacetic acid, cystine, glutamic acid, proline or tyrosine. These results were interpreted as evidence that no single amino acid can be regarded as a "key" amino acid in syntheses of hemoglobin in the organism but rather that a combination of amino acids in as yet undetermined proportions is essential for the in vivo fabrication of the hemoglobin molecule.

Fredeen, Kansas City, Mo.

Clinical Studies on Digitoxin (Digitaline Nativelle). Harry Gold, McKeen Cattell, Walter Modell, Nathaniel T. Kwit, Milton L. Kramer and William Zahm, J. Pharmacol. & Exper. Therap. **82**:187 (Oct.) 1944.

This paper is one of several from the same source on the action of digitaline and deals with its use in the treatment of more than 1,000 patients with cardiac disease. Of several specimens of digitaline Nativelle made in the laboratories of Wyeth, Incorporated, two samples ("digitoxin") were the purest and most active and were used in a large proportion of the present studies on patients. A partial summary of the paper follows.

A dose of digitaline Nativelle is equally effective by oral and by intravenous administration. This indicates complete absorption.

Digitaline Nativelle is approximately one thousand times as potent as current digitalis U. S. P. by oral administration; 1 mg. of digitaline Nativelle produces the effects of approximately 1 Gm. of digitalis.

The characteristics of the curve of cumulation and elimination of digitaline Nativelle are similar to those of the curve for digitalis.

The most favorable maintenance dose of digitaline Nativelle for routine use is 0.2 mg. daily.

A dose of 1.2 mg. of digitaline Nativelle may be given at one time with complete safety. It produces the therapeutic effects of approximately 1.2 Gm. of digitalis. The incidence of minor toxic effects is negligible with this dose, whereas its equivalent in the form of digitalis cannot be given at one time because of the frequency of gastrointestinal irritation.

Pilcher, Cleveland.

Infectious Mononucleosis Simulating Brucellosis. A. D. Rubenstein and Carolyn I. Shaw, New England J. Med. **231**:111 (July 27) 1944.

Experience with reported cases of undulant fever has demonstrated that this disease may be readily confused with infectious mononucleosis. The heterophile antibody reaction, performed routinely on 1,000 consecutive blood serums submitted by physicians for undulant fever agglutination revealed 13 cases of infectious mononucleosis. Although these specimens were submitted specifically for undulant fever only 36 were positive for that disease.

In urban areas, except for cases contracted elsewhere, undulant fever is essentially an occupational disease. Five cases of undulent fever occurred among machinists and metal workers handling materials used in processing meat products. These patients had no direct contact with animals or animal products.

To demonstrate how readily infectious mononucleosis and undulant fever may be confused, a typical case of each disease is presented. The following cases, each demonstrating an unusual feature of the respective disease, are also discussed:

infectious mononucleosis with involvement of the central nervous system, infectious mononucleosis with gastrointestinal manifestations, undulant fever of the malignant variety and undulant fever complicated by epididymitis. AUTHORS' SUMMARY.

MANIFESTATIONS OF HEMOLYTIC PHENOMENA AND INFECTIOUS MONONUCLEOSIS IN A CASE OF LYMPHATIC LEUKEMIA. FREDERIC FELDMAN and JACOB YARVIS, New York State J. Med. **44**:1693 (Aug. 1) 1944.

A case of lymphatic leukemia in an 18 year old boy is reported. In the early stages the erythrocytes showed spherocytes and a slightly increased fragility. The heterophil antibody titer was 1:1,024, and the result of the Davidson differential absorption test was indicative of infectious mononucleosis. Splenectomy was performed, and the pathologic report was consistent with a diagnosis of hemolytic icterus. After this there was a temporary improvement, but approximately six months after his admission the diagnosis of leukemia was obvious. No explanation is offered.

DAVIS, Rochester, N. Y.

EXPERIMENTS ON ERYTHROCYTE SEDIMENTATION RATE. K. MEYER, E. HAHNEL and R. R. FEINER, Proc. Soc. Exper. Biol. & Med. **58**:36 (Jan.) 1945.

The erythrocyte sedimentation rate of human blood from young healthy males was measured by the Westergren method, and no correction was made for cell volume or protein concentration. The samples were incubated for thirty minutes at 37 C. and readings made every fifteen minutes for one hour. Hyaluronic acid in particular, as well as desoxyribonucleic acid, gelatin and fibrinogen, when added to normal human citrated blood was found to cause a considerable increase in the sedimentation rate. That hyaluronic acid acts only in its highly polymerized form suggests that molecular weight, as well as asymmetry of the molecule, is an important factor. The samples of hyaluronic acid used were prepared from synovial fluid of cattle, human mesenthelioma or human umbilical cord. Further study with guinea pigs showed that hyaluronidase, prepared from ram or bull testis, specifically reverses the action of hyaluronate on the sedimentation rate. Intravenous injection of hyaluronate in the guinea pig and rabbit tends to increase the erythrocyte sedimentation rate, and intravenous injection of hyaluronidase promptly causes the increased rate to become normal.

HANSEN, Galveston, Texas.

Diseases of Lungs, Pleura and Mediastinum

THE ISOLATION OF THROMBOPLASTIN FROM LUNG TISSUE. WILLIAM H. HOWELL, Bull. Johns Hopkins Hosp. **76**:295 (June) 1945.

Although the isolation of thromboplastin in sufficient purity to determine its chemical nature was not successfully completed, it was evident that the crude material is a protein compound of a phospholipid. A method for preparation of this crude material has been perfected which gives a substance with strong thromboplastic action capable of clotting hemophilic blood in one to two minutes in concentrations of 1 mg. to 15 or 20 cc. of blood. This material can be kept in dry form in carbon dioxide with practically no loss of potency, and after sterilization by heat, in alkaline solution in sterile serum tubes with very slight loss of potency.

Material kept in liquid form in serum tubes has been used intravenously without unfavorable reactions—the material from pigs in a strain of hemophilic swine and the material from human sources in a single clinical case. This gives a definite hope that material prepared in this form may be used to control hemophilic bleeding.

Further purification of this crude material showed that it was possible to remove the protein, leaving a residue with marked thromboplastic activity, the chemical nature of which has not been determined.

AUTHOR'S ABSTRACT.

A PATIENT WITH BRONCHOPNEUMONIA TREATED BY BRONCHOSCOPIC DRAINAGE. V. LATRAVERSE and A. GUILBEAULT, Union Méd. du Canada **74**:597 (May) 1945.

An infant, 12 months old, entered the hospital with a clinical diagnosis of pneumonia. Treatment with sulfonamide compounds was started, but she showed no improvement in two weeks. Seven treatments with roentgenotherapy did not help. Even though no roentgenologic signs of atelectasis were present, bronchoscopic drainage was utilized to clear the air passages. Improvement was pronounced, and two later treatments, with concomitant instillation of 1 cc. of a 5 per cent solution of sodium sulfathiazole, sufficed to cure the condition.

DAFFINEE, Melrose, Mass.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

THE EFFECT OF PENICILLIN IN EXPERIMENTAL INTESTINAL OBSTRUCTION: PRELIMINARY REPORT ON CLOSED LOOP STUDIES. W. HENRY HARPER and ALEXANDER BLAIN III, Bull. Johns Hopkins Hosp. **16**:221 (June) 1945.

The authors studied the factors of infection in producing the toxemic symptoms occurring in intestinal obstructions without regard to the loss of fluid and electrolytes.

Of 15 dogs subjected to the "isolated obstructed loop" procedure, 87 per cent died in three and one-half days or less and 100 per cent died within six and one-half days.

In 15 dogs 50,000 units of penicillin was placed in the obstructed loops: 100 per cent were protected for nine days, 93 per cent for thirteen days and 60 per cent for over one month. In 5 dogs given penicillin parenterally 100 per cent were protected for over eighteen days.

The authors present microscopic and bacteriologic evidence to show that penicillin given in this manner can prevent infection in the distended intestinal wall by the normal intestinal flora.

LYTTLE, Los Angeles.

ULCERATIVE COLITIS. GONZALEZ AGUIRRE, B. MESSINA and O. D. VERA, Arch. argent. de pédiat. **23**:23 (Jan.) 1945.

A case of ulcerative colitis in a 9 year old boy is reported. The first signs appeared at 6 months of age, and except for a period of twelve months, during which he was free of symptoms, clinical manifestations have been present ever since.

The diagnosis was made after careful clinical and laboratory examinations, including roentgenographic and rectoscopic studies. At the time the article was written, the child appeared malnourished and undersized. Several therapeutic procedures were carried out, to no avail.

The authors review the literature, with particular reference to the work of Jackman, Bargen and Helmholz (Life Histories of Ninety-Five Children with Chronic Ulcerative Colitis, AM. J. DIS. CHILD. **59**:459 [March] 1940).

Treatment is thoroughly discussed, the conclusion being that one should exhaust medical treatment before resorting to surgical intervention.

CASSORLA, Chicago.

Psychology and Psychiatry

A Psychiatric Adventure in Comparative Pathophysiology of the Infant and Adult. J. J. Michaels, J. Nerv. & Ment. Dis. **100**:49 (July) 1944.

The author presents a philosophic discussion of psychosomatic implications from birth through adulthood with particular reference to the emotional expression at various age levels and the reactions to physiologic demands and physiologic disturbances. This paper should be read in its original form. Jahr, Omaha.

The Place of Elements Teaching in Speech Development: Is the Cart Before the Horse? M. E. Numbers, Volta Rev. **44**:261, 1942.

The author believes that the method of speech teaching which consists in teaching first the consonants and vowels as separate elements, often as mere positions of the vocal organs, and insisting that pupils master these individual sounds before combining them into syllables is based on an inadequate knowledge of the processes involved in speech production. This method ignores the important fact that a vital portion of the speech mechanism lies below the level of the larynx. Pupils called on to combine elements into words and phrases are required to bring into play an entire set of muscles which have not entered into the training process. A method of teaching speech by syllables is advocated in which the elements are associated from the beginning in the relationships in which they appear in normal speech. The elements, or individual sounds, are thus not ignored but, rather, are taught as vital parts of an integrated whole. [Angle Orthodontist]

Extraschool and Postschool Education. Estela Meguira, Bol. Inst. internac. am. de protec. a la infancia **18**:401 (Sept.) 1944.

In order to encourage the education that could be attained through reading, the following objections should be borne in mind:

1. To teach how to read and to interpret what is read. This mission belongs to the school, which should give special attention to methods employed in the initiation of reading in order to attain the development of the mind of the future reader.

2. To favor a campaign in behalf of good books to be used as school reading textbooks.

3. To give special attention to the appearance of the books presented to the child and the adolescent, to favor the distribution of books and at the same time, to try to obtain as low a cost as possible.

4. To encourage the development of literature for children and juveniles and the organization of periodic competitions among authors.

5. To organize competitions among the small readers.

6. To exercise control of the contents of periodicals and leaflets offered to children and adolescents.

7. To encourage the organization of libraries with particular features, as well as the coordination of private and public action.

8. To attempt the establishment of circulating libraries for the rural environment.

9. To give special training to the librarian and the assistants of libraries for children.

Moreover, the author states that it is of great importance that the government give special attention to the study of best employment of the leisure time of children and adolescents, for it embraces extraschool and postschool education.

In the words of Mrs. Frances Perkins, at the opening session (Jan. 18, 1940) of the White House Conference on Children in a Democracy: "One of the problems in this as well as in every other nation is how to make it possible for children,

who are the future generation, to partake of the best that the nation is able to give while they are children, while they are in the formative stage, while their health is being built up."

AUTHOR'S SUMMARY.

Diseases of the Ductless Glands; Endocrinology

OBSERVATIONS ON SOME HISTOCHEMICAL REACTIONS IN THE HUMAN PLACENTA, WITH SPECIAL REFERENCE TO THE SIGNIFICANCE OF LIPOIDS, GLYCOGEN AND IRON. EDWARD W. DEMPSEY and GEORGE B. WISLOCKI, Endocrinology **35**: 409 (Dec.) 1944.

In this paper are reported the results obtained by the application of a number of histochemical reactions to human placental tissue. These reactions centered around the localization of lipids, glycogen and iron.

It is indicated that the syncytium is the site of localization of the placental steroid hormones.

From consideration of glycogen distribution in various tissues, both fetal and adult, the concept is developed that deposition of glycogen is generally associated with anaerobic conditions and that, through anaerobic breakdown, it may provide a mechanism for the oxidative reactions of tissues in which the oxygen supply is deficient.

The syncytium of the early placenta contains considerable quantities of iron, whereas in later stages of pregnancy the amount is greatly reduced.

JACOBSEN, Buffalo.

DIABETES IN A TOTALLY DEPANCREATIZED MAN. HENRY T. RICKETTS, ALEXANDER BRUNSCHWIG and K. KNOWLTON, Proc. Soc. Exper. Biol. & Med. **58**:254 (March) 1945.

It was necessary to resect the entire pancreas in a man with a carcinoma of the pancreas. He had had abdominal pain and diarrhea for two years and had manifested symptoms of diabetes mellitus nine months previously. In addition to removal of the entire pancreas, the duodenum, stomach, spleen, left adrenal gland and most of the omentum were removed. The liver appeared normal. Histologic examination of the head of the pancreas, which was free from carcinoma, showed insular changes characteristic of diabetes. The patient lived fourteen weeks. Before operation 40 to 65 units of insulin was required to keep the urine free from sugar, the dextrose equivalent of the diet being 511 Gm., while two months after the operation the insulin requirement was about 40 units, the dextrose equivalent of the food being 459 Gm. The weight of the patient was 72 Kg. before operation and 56 Kg. at the time of the subsequent study, two months later. The patient had frequent hypoglycemic reactions, and apparently he showed pronounced sensitivity to insulin. The authors note the striking fact that the insulin requirement was extremely low in this totally depancreatized man and that the insulin output daily must be considered to be but 30 to 50 units. Therefore they believe that in diabetic patients requiring more than this amount of insulin there is an extrainsulin factor contributing to the diabetic syndrome. In this fasting depancreatized man with no insulin protein was converted to carbohydrate at a rate commensurate with that of the depancreatized dog under the same conditions.

HANSEN, Galveston, Texas.

THE STABILIZATION OF THE INSULIN DOSAGE IN FRESH DIABETES IN CHILDHOOD. ARNE ROTHE MEYER, Nord. med. (Hygiea) **24**:2234 (Dec. 15) 1944.

Fifty diabetic children, all of them treated without diet and with protamine insulin or protamine zinc insulin, have been followed for a suitable period after the first treatment. It was found that 15 children reached a constant level of insulin

within two months after the beginning of treatment with insulin, while 30 children had attained this level within six months. In only 5 children was the stabilization manifest after more than twelve months. The insulin levels below 30 units showed a tendency toward a shorter initial period than the levels above 30 units. There was no relation between the age of the child at the onset of the disease and the duration of the labile period.

WALLGREN, Stockholm, Sweden.

Skin Diseases; Allergy

KAPOSI'S VARICELLIFORM ERUPTION: EXTENSIVE HERPES SIMPLEX AS A COMPLICATION OF ECZEMA. FRANCIS W. LYNCH, C. A. EVANS, VERNON S. BOLIN and RICHARD J. STEVES, Arch. Dermat. & Syph. **51**:129 (Feb.) 1945.

The virus of herpes simplex may become implanted on previously disturbed skin, the most frequent disturbance being eczema, and Kaposi's varicelliform eruption is produced. The condition may be mistaken for eczema vaccination, but it may be differentiated by the presence of herpes simplex in either parent or on the lips of the child and by absence of recent vaccination. The implantation causes an acute vesiculation of the eczematous areas of the skin and a severe systemic reaction, both of which abate in a few days. The authors describe 4 cases, 2 of which were of children who suffered from atopic eczema.

MCINTOSH, Iowa City.

STUTTERING. I. W. CARLIN, Arch. Pediat. **63**:23 (Jan.) 1946.

The author discusses stuttering as primarily a pediatric problem and one which should be treated as soon as discovered. Theories of its causation are discussed. He points out that attempts at relating speech difficulty to endocrine disorders, biochemical imbalances and laterality tendencies have been of little help and that therapy must be primarily directed toward emotional and psychologic problems.

GRULEE JR., Minneapolis.

CONDITION OF CHILDREN IN FRANCE UNDER THE OCCUPATION. ROBERT DEBRE, Proc. Roy. Soc. Med. **38**:447 (June) 1945.

In 1940, when there was a mass exodus of French people because of the approaching Germans, the children suffered severely from lack of food and shelter and on their return found food supplies rigidly controlled by the Germans, who issued meager rations for the children. Fuel and light were limited; shoes and clothes wore out and could not be replaced. Many families spent sleepless nights in terror of police raids. During the war birth weights were lower. In the Parisian district, breast nursing increased from 35 per cent to 90 per cent; hence the babies did well for the first six months of their lives. During the four years of German occupation children managed to receive their milk, but the animal proteins needed for their growth were practically impossible to obtain.

The food situation since the Liberation has grown worse. Milk to children over 1 year is no longer allowed. All school children have lost weight. Psychologic reactions in young children are very evident. Infectious diseases, cutaneous diseases, digestive troubles and tuberculosis have all increased. In all of this it is obvious that malnutrition plays a large part. French children were subjected to brutalities during the occupation. Hundreds of young women gave birth to their children in prison, and the children were never seen. The ghastly story of Oradour is well known. Whole families, including children, were shot in many villages.

WILLIAMSON, New Orleans.

CHILD LIFE AND HEALTH IN BELGIUM DURING AND AFTER THE GERMAN OCCUPATION. R. W. B. ELLIS, Proc. Roy. Soc. Med. **38**:449 (June) 1945.

The German occupation of Brussels lasted from May 1940 to September 1944. By means of a restrospective survey in the winter of 1944-1945, an attempt was made to determine the effect of the occupation on the children of Belgium. From a psychologic aspect the opinion was formed that the effect on the children had been much less than on their parents. The nutrition of the younger children was maintained at the expense of the older children and adults. The chief deficiencies in the diet, apart from total calories, were fat and first class protein. There do not appear to have been any large scale epidemics during the war. There was an increase in impetigo, scabies and osteomyelitis secondary to cutaneous sepsis (due to lack of soap and fuel).

Dr. Ellis has presented a detailed study of a working class family with three children.

WILLIAMSON, New Orleans.

SCLERODERMA. LORENZO EXPOSITO, A. DE FERIA SANTIESTEBAN and J. BARQUET, Bol. Soc. cubana de pediat. **16**:179 (May) 1944.

This article is a review of the whole subject of scleroderma at some length. Four cases are reported, in 3 of which biopsy of the skin is reported on.

KEITH, Rochester, Minn.

Surgery and Orthopedics

SPINAL ANALGESIA IN THE VERY YOUNG AND FURTHER OBSERVATIONS. W. ETHERINGTON-WILSON, Proc. Roy. Soc. Med. **38**:109 (Jan.) 1945.

Ten years ago the author read a paper and showed a long film concerned with the anatomic, physical and experimental aspects of spinal analgesia (*Proc. Roy. Soc. Med.* **27**:323, 1934).

In the present paper he reports on a careful record of 1,600 supervised cases. He devotes a paragraph to spinal analgesia in babies and indicates the following points requiring attention: (1) dosage and timing (see formula table); (2) care, knowledge and understanding on the part of the theater staff; (3) suitable preoperative preparation; (4) use of nupercaine hydrochloride in 1:2,500 or 1:2,000 dilution and a no. 16 hypodermic needle for lumbar puncture (insertion in fourth interspace); (5) appearance of signs of anesthesia soon after timing in the vertical position and the assumption of the Trendelenburg position; (6) use of nasal oxygen. In some cases in which a drip transfusion was not used a stimulant was given.

The advantages of spinal analgesia are evident, e. g., perfect relaxation, no protrusion of the small gut, incision, no haste, less loss of blood and better healing of the wound. After operation, placing in the Trendelenburg position and continued use of warmth and fluid drips are necessary precautions.

In conclusion, the author points out some of the advantages of spinal analgesia for the surgeon, the patient, the nursing staff and the anesthetist.

WILLIAMSON, New Orleans.

Teeth and Dentistry

A SURVEY OF NEEDS AND SERVICES AVAILABLE FOR PROTECTIVE DENTISTRY FOR THE INDIGENT CHILDREN AND YOUTH IN THE U. S. A. ALAN E. TRELOAR, J. Am. Dent. A. **31**:326, 1944.

This is a supplement to a report by Brekhus and associates. An estimated cost of $40,297,984 per year for the country as a whole to provide protective dentistry for the indigent child population, 6 to 18 years of age, was obtained from the following sources of data: the United States Census of 1940, the number of

registered dentists in each state for the year 1940 and a number of studies (not mentioned by title or author) on the incidence of dental caries in the age group 6 to 18 years in the United States. The figure of 1 carious tooth per child per year, at the cost of $4.00, is used as a basis for determining the maximum load and cost to be anticipated.

[ANGLE ORTHODONTIST]

Miscellaneous

EFFECTS OF ENZYME PREPARATIONS UPON PENICILLIN: I. A METHOD FOR TESTING PENICILLIN FOR STERILITY. C. A. LAWRENCE, J. Bact. **49**:47 (Jan.) 1945.

All the methods that have been used in testing penicillin for sterility have included various enzyme preparations, for they appeared to meet the requirements for inactivating the antibiotic substance. The author found that with one exception the enzymes showing antipenicillin effects were the products taka-diastase and clarase, both of which are derived from the fungus Aspergillus oryzae. The exception was a bacterial enzyme preparation from Bacillus mesentericus. It neutralized the antibacterial effects of penicillin.

Other diastatic enzymes, including several also derived from A. oryzae, as well as a group of proteolytic enzymes, did not show any evidence of an antipenicillin effect.

A test for sterility of penicillin using solutions of a highly active, antipenicillin preparation of clarase is presented by the author, and the original paper should be consulted for details.

STOESSER, Minneapolis.

THE PROLONGING ACTION OF PENICILLIN BY PARA-AMINOHIPPURIC ACID. L. LOEWE, P. ROSENBLATT, E. ALTURE-WERBER and M. KOZAK, Proc. Soc. Exper. Biol. & Med. **58**:298 (April) 1945.

Four human subjects with subacute bacterial endocarditis were given 40 to 80 Gm. of para-aminohippuric acid with 500,000 to 2,000,000 Oxford units of penicillin intravenously, and the blood levels of these substances were studied for various periods up to eight days in length. When the para-aminohippuric acid level exceeded 10 mg. per hundred cubic centimeters of serum, a threefold to sixfold increase in the plasma levels of penicillin was observed, whereas when the para-aminohippuric acid levels were below this value the plasma level of penicillin was little affected. Patients given para-aminohippuric acid expressed a feeling of restlessness and warmth, palpitation or desire to urinate and defecate, but these symptoms were all mild.

HANSEN, Galveston, Texas.

THE SICK INFANT. GRACIA SCAFFO DE CASAS MELLO, Bol. Inst. internac. am de protec. a la infancia **18**:655 (Dec.) 1944.

To prevent in part the suffering of infants, the following measures are necessary: (1) training of mothers in order to develop in them maternal understanding; (2) education of the community concerning the duties that should be fulfilled with respect to children; (3) establishment of health centers for mothers and children, for, as Professor Morquio has said, "Infants should be trained from the time of birth; diseases should be avoided; their hygienic state should be taken care of; mothers should be protected, and their economicosocial problems should be solved by legislation." Thus, real prophylaxis and effective protection of infants would be obtained.

AUTHOR'S SUMMARY.

Book Reviews

What People Are: A Study of Normal Young Men. By Clark W. Heath, M.D., in collaboration with Lucien Brouha, Lewise W. Gregory, Carl C. Seltzer, Frederic L. Wells and William L. Woods, M.D. The Grant Study, Department of Hygiene, Harvard University. Price, $2. Pp. 141, with 7 tables and 8 figures. Cambridge, Mass.: Harvard University Press, 1945.

This book is an introduction to the point of view of the Grant Study supported by the Grant Foundation, Inc., New York. It is a study of normal young men, whose careers will be followed for fifteen or twenty years. The approach is stated to be clinical and is presented in three sections, with appendixes presenting the assembled data.

The introduction defines "normal" in its broadest sense and points out the need for the study in determining factors which make for leadership, as well as other factors that make for happier and more successful lives.

The nature of approach, the organization and general plan of work selection and methods of examining participants are also discussed in the introduction.

In the next section of the book the method, the approach and a description of normal young men from the angle of different disciplines are presented. Soundness is used as a basis of classification, the classes A, B and C being defined as follows: A, young men thoroughly sound; B, boys with a question of a minor flaw, and C, boys whose history reveals a definite handicap.

The different disciplines used in the description of the normal are: personality, manner of adjustment to certain conditions, socioeconomic observations and morphologic, physiologic, medical and mental measurements.

Of special interest is the description of the manner of adjustment to certain common conditions that confront almost any young man, adjustment to any of which is often something of a "problem." In this category are such "problems" as choice of a career, participation in athletics, religion and sex. The students were separately interviewed in sincere and open discussions.

Data assembled from these approaches are presented in eight appendixes. The tables and illustrations also show the results of some of the studies.

The work is unusual, and the new approach is refreshing in its broadness, its interpretation and its vision.

The Chemistry and Technology of Food and Food Products. Prepared by a Group of Specialists Under the Editorship of Morris B. Jacobs, Ph.D., Senior Chemist, Department of Health, City of New York. Volume II. Cloth. Price $10.50; $19 per set of two volumes. Pp. 890, with 166 illustrations. New York: Interscience Publishers, Inc., 1944.

This is the second of two volumes in which forty-one scientists have collaborated to present an authoritative work on food. Food technologists, chemists, biochemists, bacteriologists, sanitary engineers and others have each written on the phase of food chemistry and technology which he was best qualified to discuss. Volume I contains parts 1 and 2, covering fundamental information about food, as well as its history, standards, composition and place in nutrition.

This volume, containing the remaining four parts, covers the technologic problems of foods. Theoretic and practical food processing, equipment and materials are discussed in part 3. How government agencies (national, state and local) function in protecting health and preventing fraudulent and unfair practices as well as promoting industry and trade is explained.

Quality and sanitary control through food grading is covered in some hundred and fifteen pages of part 4. Food equipment, its care and sanitation is also presented.

Methods of food preservation, including chapters on dehydration, refrigeration, cold storage, freezing, canning and fermentation and salting, as well as chemical preservatives, are covered in considerable detail in part 5. The processing of all types of foods, such as cereals, breads and other baked products, sugars, confectionery products, milk, meat and beverages, is presented in the more than four hundred pages of part 4.

Any one needing concise information about foods that is not too technical should find this set of books helpful as a reference text. The selected bibliography at the end of each chapter will guide the person wanting more detailed information. These books are well indexed, making it simple to find information desired. Persons interested in foods will find this set of books a valuable addition to their reference library.

News and Comment

GENERAL NEWS

Malignant Tumors of Infancy and Childhood—Organization of a New Consultation Service.—Announcement is made of establishment of a consultation service to provide assistance in the diagnosis and treatment of tumors of infancy and childhood. This is a further step in the organization of a Children's Cancer Center, which is a unit of the new Medical Center for Children in Boston.

This is not a tumor registry. It is designed, rather, to give without charge immediate diagnostic assistance and advice concerning therapy and prognosis to any doctor who will send the necessary clinical data, microscopic sections or roentgenograms. Replies will be given by air mail, or when necessary by telephone or telegraph. This project, which is supported in part by a grant-in-aid from the National Advisory Cancer Council, will be paralleled by a research program concerning the biology of tumors of early life, with a consideration also of the clinical, pathologic and epidemiologic aspects of the problem.

The consultation service will be rendered by a group of three pathologists, Dr. S. Burt Wolbach, Dr. Charles F. Branch and Dr. Sidney Farber, and by one roentgenologist, Dr. Edward B. D. Neuhauser, with the cooperation when indicated of the entire staff of The Children's Hospital, through the chiefs of the clinical services. Doctors representing all the clinical and laboratory specialties concerned with the infant or the child will be available for consultation.

Communications should be sent to Dr. Sidney Farber, The Children's Hospital, 300 Longwood Avenue, Boston 15, Mass., beginning Aug. 1, 1946.

Changes at University of Tennessee College of Medicine.—Dr. E. C. Mitchell has been appointed emeritus professor of pediatrics at the University of Tennessee College of Medicine and has been succeeded by Dr. F. T. Mitchell as professor of pediatrics and head of the department. Dr. James G. Hughes has been promoted to associate professor of pediatrics.

New Appointment for Dr. Hart E. Van Riper.—Dr. Hart E. Van Riper, who was formerly with the Children's Bureau and later at the Jackson Memorial Hospital in Miami, Fla., has been made assistant medical director of the National Foundation for Infantile Paralysis, Inc., and will be assistant to Dr. Don W. Gudakunst.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-General: Dr. L. Emmett Holt Jr., 477 First Ave., New York 16.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto 2.
Secretary: Dr. H. P. Wright, 1414 Drummond St., Montreal.
Place: New York. Time: Postponed indefinitely.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

Save the Children International Union

President: Mrs. Gordon Morier.
Secretary: Dr. Georges Thélin, 43 Quai Wilson, Geneva, Switzerland.
Place: Geneva, Switzerland. Time: Sept. 17-20, 1946.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

Associação Paulista de Medicina, Secção de Pediatrias

President: Dr. Vicente Lara.
First Secretary: Dr. Armando de Arruda Sampaio.
Second Secretary: Dr. Luiz Augusto Monteiro Toledo, Av. Brigadeiro Luiz Antonio 393, 1° Andar, São Paulo, Brazil.
Time: Twelfth of every month, 8:30 p. m.

British Paediatric Association

President: Prof. G. B. Fleming, 13 Lynedoch Crescent, Glasgow.
Joint Secretary: Prof. Alan Moncrieff and Dr. Donald Paterson, Hospital for Sick Children, Great Ormond St., London, W. 1.
Place: Rugby School, Rugby. Time: Aug. 1-3, 1946.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Nederlandische Vereeniging voor Kindergeneeskunde

President: Dr. J. H. G. Carstens, Servaas Bolwerk 14, Utrecht.
Secretary: Dr. R. P. van de Kasteele, Lyccumplein 10, den Haag.
Place: Children's Hospital or Pediatric Clinic. Time: Three times a year.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. L. F. Meyer, 29 Toelsohn St., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASE IN CHILDREN

President: Prof. Norman Capon, 49A Rodney St., Liverpool, England.
Secretary: Dr. J. N. O'Reilly, 46 Harley St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

SOCIEDAD CUBANA DE PEDIATRIA

President: Dr. Teodosio Valledor, Habana.
Secretary: Dr. Carlos Hernandez Miyares, Hospital Nuestra Señora de las Mercedes L y 21, Apartado, 2430, Habana.
Place: Cátedra de Clinica Infantil, Hospital Nuestra Señora de las Mercedes y Hospital Municipal de Infancia, Habana. Time: Last Wednesday of every month.

SOCIEDAD ECUADORIANA DE PEDIATRIA

President: Dr. Francisco de Icaza Bustamente.
Secretary: Dr. M. I. Gómez Lince, P. O. Box 693, Guayaquil.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Fernando López Clares, 12/a. Medellín 191, Mexico.
Secretary: Dr. Jesus Gómez Pagola, Versalles 64, Mexico.

SOCIEDAD DE PEDIATRIA DE CÓRDOBA

President: Dr. Juan Francisco Herrera, Córdoba, Argentina.
Secretary: Dr. Bernardo Serebrinsky, Dean Funes 2000, Esq. Ocaña (N.), Córdoba, Argentina.

SOCIEDAD DE PEDIATRÍA DE SANTIAGO DE CUBA

President: Dr. Antonio Béguez César, Sagarra 107, Santiago de Cuba.
Secretary: Dra. Susana Texdó Vaillant, Padre Pico 57, Santiago de Cuba.
Place: Colegio Médico. Time: Last Tuesday of every month.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRIA

President: Dr. Pedro J. Alvarez.
Secretary: Dr. Ernesto R. Figueroa, 3a Avenida 10, Bella Vista, Caracas.
Place: Hospital Municipal de Niños Jose Manuel de los Rios, Caracas.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. Leveuf, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Maladies, 149 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

URUGUAYAN SOCIETY OF PEDIATRICS

President: Dr. Jose Bonaba, Montevideo.
Secretary: Dr. Héctor Fossatti, Durazno 1882, Montevideo.
Place: Club Medico del Uruguay, Avenida Agraciado 1464 (Piso 13), Montevideo.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blvd., Memphis, Tenn.
Place: San Francisco. Time: July 1-5, 1946.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. Jay I. Durand, 515 Cobb Bldg., Seattle, Wash.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Hotel William Penn, Pittsburgh. Time: Nov. 13-16, 1946.
Region I. Place: Hotel Pennsylvania, New York. Time: April 2-4, 1946.

AMERICAN HOSPITAL ASSOCIATION, MASSACHUSETTS HOSPITAL ASSOCIATION

Chairman: Dr. Mr. Frank Wing, Boston.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly 79, Mass.
Place: Boston. Time: November 1946.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Harold K. Faber, 2361 Clay St., San Francisco.
Secretary-Treasurer: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. H. S. Little, 300 Dufferin Ave., London, Ontario.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, 67 College St., Toronto 2.
Place: Banff, Alberta. Time: June 14-15, 1946.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia 46.
Secretary: Dr. Robert F. Ward, Bellevue Hospital, New York.

SECTIONAL

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Robert Alway, University of Utah School of Medicine, Salt Lake City 2.
Secretary-Treasurer: Dr. L. Paul Rasmussen, 1020 Boston Bldg., Salt Lake City 1.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. William P. Buffum, 122 Waterman St., Providence, R. I.
Secretary-Treasurer: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Three meetings a year, occurring from September to May.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. Percy Guy, 502-2d Ave., Seattle, Wash.
Secretary: Dr. Aldis B. Johnson, 515 Cobb Bldg., Seattle, Wash.
Place: Vancouver, B. C. Time: Oct. 19, 1946.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. George B. Logan, 102 Second Ave. S. W., Rochester, Minn.
Secretary-Treasurer: Dr. Northrop Beach, 1009 Nicollet Ave., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. G. R. Fisher, 23 E. Pikes Peak Ave., Colorado Springs, Colo.
Secretary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver 2.

SOUTHERN MEDICAL ASSOCIATION, SECTION OF PEDIATRICS

Chairman: Dr. William Weston Jr., 1428 Lady St., Columbia, S. C.
Secretary: Dr. Angus McBryde, 604 W. Chapel Hill St., Durham, N. C.

STATE

Alabama Pediatric Society

President: Dr. Jerome C. Chapman, 2160 Highland Ave., Birmingham.
Secretary-Treasurer: Dr. Ruth Berrey, 2021–6th Ave. N., Birmingham.
Place: Birmingham. Time: September 1946.

Arizona Pediatric Society

President: Dr. Vivian Tappan, San Clemente, Tucson.
Secretary: Dr. Hilda Kroeger, Arizona State Health Dept. (Maternal and Child Welfare Division), Phoenix.
Place: Phoenix or Tucson. Time: At time of state meeting.

Arkansas State Pediatric Association

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

California State Medical Society, Section on Pediatrics

Chairman: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco 9.
Secretary: Dr. Chester I. Mead, 1930 Truxton Ave., Bakersfield.
Place: Biltmore Hotel, Los Angeles. Time: May 7-10, 1946.

Florida State Pediatric Society

President: Dr. Councill Rudolph, 103–5th St. S., St. Petersburg.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association convention and fall meeting.

Georgia Pediatric Society

President: Dr. Alton Johnson, 102 E. Central Ave., Valdosta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Place: Atlanta. Time: At time of annual state meeting.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. Edward T. Wakeman, 129 Whitney Ave., New Haven.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.
Place: New Haven. Time: September 1946.

Illinois State Medical Society, Section on Pediatrics

Chairman: Dr. Craig D. Butler, 715 Lake St., Oak Park.
Secretary: Dr. A. J. Fletcher, 139 N. Vermilion, Danville.

Indiana State Pediatric Society

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Matthew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.
Secretary-Treasurer: Dr. James Dunn, 414 Blackhawk Hotel, Davenport.
Place: Des Moines. Time: April 18, 1946.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn, N. Y.
Secretary: Dr. George R. Murphy, 292 Madison Ave., New York.
Place: Hotel Pennsylvania, New York. Time: May 2-3, 1946.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary: Dr. P. F. Lucchesi, Philadelphia Hospital, Philadelphia.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Donald J. Barnes, 3001 W. Grand Blvd., Detroit, Mich.
Secretary: Dr. Mark F. Osterlin, Central Michigan Children's Clinic, Traverse City.
Place: Detroit. Time: Sept. 25-27, 1945.

Mississippi State Pediatric Society

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

Nebraska Pediatric Society

President: Dr. John M. Thomas, 1418 Medical Arts Bldg., Omaha 2.
Secretary-Treasurer: Dr. Gerald C. O'Neil, 640 City National Bank Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

New Mexico State Pediatric Society

President: Dr. M. K. Wylder, 221 W. Central Ave., Albuquerque.
Secretary-Treasurer: Dr. Ly Werner, 221 W. Central Ave., Albuquerque.

North Carolina Pediatric Society

President: Dr. Charles R. Bugg, Profesional Bldg., Raleigh.
Secretary: Dr. Charles F. Williams, 817 Hillsboro St., Raleigh.
Place: Roaring Gap. Time: September 1946.

Northern California Pediatric Society

President: Dr. Edith M. Meyers, 431–30th St., Oakland.
Secretary: Dr. A. L. Gleason, 411–29th St., Oakland 9.
Place: San Francisco. Time: Second Thursday of February, April, September and November.

Oklahoma State Pediatric Society

President: Dr. G. R. Russell, 604 S. Cincinnati Ave., Tulsa.
Secretary: Dr. Luverne Hays, 108 W. 6th St., Tulsa.
Place: With Oklahoma State Medical Association. Time: Annual Meeting.

South Carolina Pediatric Society

President: Dr. George D. Johnson, Spartanburg.
Secretary-Treasurer: Dr. B. O. Ravenel, Roper Hospital, Charleston:

Texas Pediatric Society

President: Dr. Max Woodward, 202 N. Travis St., Sherman.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas 4.
Place: Fort Worth. Time: Oct. 4-5, 1946.

Virginia Pediatric Society

President: Dr. Emily Gardner, 1100 W. Franklin St., Richmond 20.
Secretary: Dr. Louise Galvin, 214 S. Boulevard, Richmond 21.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. Jack Basman, 1021 Quarrier St., Charleston.
Secretary: Dr. Harry E. Baldock, Medical Arts Bldg., Charleston.
Place: Huntington. Time: May 13-15, 1946.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. I. Hartman, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. Alexander N. Freed, 2012 W. 25th St., Cleveland.
Place: Cleveland Medical Library Bldg. Time: 8:15 p. m., October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. J. H. Ebbs, 13 Queen's Park, Toronto, Canada.
Secretary: Dr. J. F. McCreary, 170 St. George St., Toronto, Canada.
Place: Academy of Medicine. Time: 8:30 p. m., third Thursday of each month.

Bronx Pediatric Society

President: Dr. Walter Levy, 12 E. 88th St., New York.
Secretary: Dr. Joseph Blasenstein, 960 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Lambert Krahulik, 14 Sidney Pl., Brooklyn.
Secretary: Dr. Joseph Battaglia, 713 Bushwick Ave., Brooklyn 21.
Place: Granada Hotel. Time: 8:45 p. m. fourth Wednesday of February, March, April, May and November.

Buffalo Pediatric Society

President: Dr. Douglas P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo 9, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

Central New York Pediatric Club

President: Dr. Arthur W. Benson, 2 St. Paul St., Troy.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and October.

Chicago Pediatric Society

President: Dr. Louis W. Sauer, 636 Church St., Evanston, Ill.
Secretary: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May inclusive.

Cincinnati Pediatric Society

President: Dr. Theodore K. Selkirk, 3605 Edwards Rd., Cincinnati.
Secretary: Dr. John H. Hunt, Kemper Lane Bldg., Cincinnati 6.
Place: Children's Hospital, Elland Ave., Cincinnati. Time: On call.

Dallas Pediatric Society

President: Dr. O. René Caillet, 4325 Cole Ave., Dallas, Texas.
Secretary-Treasurer: Dorothy Wyvell, Bradford Memorial Hospital for Babies, Texas.
Place: Children's Medical Center. Time: 1 p. m., third Saturday and 8:30 p. m. the first Thursday of each month.

Detroit Pediatric Society

President: Dr. Philip J. Howard, 2977 W. Grand Blvd., Detroit, Mich.
Secretary: Dr. John C. Montgomery, 773 Fisher Bldg., Detroit 2, Mich.
Place: Variable. Time: Five times a year.

Houston Pediatric Society

President: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd., Houston, Texas.
Place: River Oaks Country Club. Time: 7:30 p. m., fourth Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1624 Professional Bldg., Kansas City.
Secretary: Dr. Leland Speer, 1022 Parkway, Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Milo B. Brooks, 1033 Gayley Ave. W., Los Angeles.
Secretary-Treasurer: Dr. Elena Boder, 1830½ Lucille Ave., Los Angeles 26.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Abraham M. Litvak, 1145 Eastern Parkway, Brooklyn.
Secretary: Dr. Harold Levy, 750 St. Marks Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m. fourth Monday of each month.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. Meyeron Coe, 217-02-91st Ave., Queens Village, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144-38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. John Washington, 2203 Wyoming Ave., Washington, D. C.
Secretary-Treasurer: Dr. George Maksim, 1418 Good Hope Rd. S.E., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., third Thursday of October, January, March and May.

Memphis Pediatric Society

President: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Barton Etter, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis Country Club. Time: 8 p. m., Dec. 13, 1946.

Milwaukee Pediatric Society

President: Dr. G. H. Fellman, 231 W. Wisconsin Ave., Milwaukee.

Secretary-Treasurer: Dr. R. P. Showalter, 411 E. Mason St., Milwaukee 2.

Place: Milwaukee Children's Hospital. Time: Second Wednesday in February, April, June, October and December.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Alfred E. Fischer, 73 E. 90th St., New York.

Secretary: Dr. Robert O. Du Bois, 122 E. 76th St., New York.

Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Oklahoma City Pediatric Society

President: Dr. William M. Taylor, 625½ N. W. 10th St., Oklahoma City.

Secretary: Dr. Jeanne McKinnon-Shofstall, 1019 N. Lee St., Oklahoma City.

Place: Oklahoma Club. Time: Third Thursday of each month.

Philadelphia Pediatric Society

President: Dr. Waldo E. Nelson, Temple University School of Medicine, Philadelphia.

Secretary: Dr. Sherman Little, 1740 Bainbridge St., Philadelphia 46.

Place: College of Physicians, 19 S. 22d St. Time: 8:30 p. m., second Tuesday in October, December, February and April.

Pittsburgh Pediatric Society

President: Dr. Elwood Stitzel, 403 Central Trust Bldg., Altoona, Pa.

Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh 13.

Place: Pittsburgh Academy of Medicine. Time: Second Friday in October, December, February and April.

Richmond Pediatric Society

President: Dr. Edwin L. Kendig Jr., 828 W. Franklin St., Richmond 20, Va.

Secretary-Treasurer: Dr. Thomas S. Chalkley, 1200 E. Broad St., Richmond, Va.

Place: Medical College Hospital. Time: 8 p. m., third Thursday of each month. except June, July and August.

Rochester Pediatric Society

President: Dr. William L. Bradford, 260 Crittenden Blvd., Rochester 7, N. Y.

Secretary-Treasurer: Dr. Donald D. Posson, 222 Chili Ave., Rochester 11, N. Y.

Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May.

St. Louis Pediatric Society

President: Dr. Joseph C. Jaudon, 337 N. Euclid Ave., St. Louis.

Secretary-Treasurer: Dr. Gilbert B. Forbes, 500 S. Kingshighway, St. Louis 10.

Time: Second Thursday of each month from October to May, inclusive.

Seattle Pediatric Society

President: Dr. D. M. Dayton, 740 St. Helens Ave., Tacoma.

Secretary: Dr. W. B. Chesley, 1306 Madison St., Seattle 4.

Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Robert J. Dostal, 710 Wilshire Blvd., Santa Monica, Calif.

Secretary: Dr. H. M. Van Dyke, 541 E. Broadway, Long Beach, Calif.

Place: University Club of Los Angeles. Time: 6:30 p. m., first Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Park Bradshaw, Muskegon, Mich.

Secretary: Dr. Harry A. Towsley, 1313 E. Ann St., Ann Arbor, Mich.

Place: University Hospital, Ann Arbor, Mich. Time: Oct. 25-26, 1946.

Westchester County Medical Society, Pediatrics Section (New York)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.

Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.

Place: Hospitals of Westchester County. Time: Third Thursday in November, January, March and May.